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Original Communications

ANATOMIC VARIATIONS OF THE VAGUS NERVS— THEIR SIGNIFICANCE IN VAGUS NEURECTOMY

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NEW YORK N Y

DURING recent years there has been an increasing interest in the role of the psychic factors in peptic ulcer. The degree of the psychic influence is not known but that it is of importance is generally accepted today. On the assumption that the psychic factors as contributors to the cause and continuation of chronicity of peptic ulcers are mediated through the vagus nerves it has been thought logical also to assume that interruption of the vagus nerves would curtail the added gastric secretions and motility. In contradistinction to the earlier views of Beaumont and Pavlov, that in the absence of food or psychic stimuli the gastric glands are quiescent the work of Carlson¹ indicates that there is a continuous secretion of gastric juice in the normal individual and that this occurs even in prolonged fasting. Thornton Storer and Dragstedt² have shown that there is an abnormality in the secretion of gastric juice in most if not all ulcer patients, the continuous secretion being abnormally high in the absence of stimulation by food or psychic factors and they further state that the most pronounced increase over the normal is noted in the volume and acidity of the continuous night secretion. There is also excessive motility of the stomach in many ulcer patients and both contribute to the cause and maintenance of chronicity of peptic ulcers. Both hypermotility and hypersecretion the latter the more important of the two are diminished following section of the vagus nerves.

Early descriptions of vagotomies for various therapeutic purposes were reported by Exner and Schwartzman in 1912, Sterling³ in 1920, Latarjet and Burcher in 1921 and Schuss⁴ in 1923. Most if not all of these vagotomies were incomplete. Hartzell⁵ in 1929 reported a decrease in acid secretion following intrathoracic complete vagotomy in dogs. Wilhelm McCarthy, and Hall⁶ performed partial gastrectomy and complete vagotomy on four dogs in 1936.

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just below the lung root to the mid portion of the gastric fundus. Transthoracic vagotomy is at present being used more widely than the transabdominal approach, although Dragstedt and his co-workers have had wide experience with both approaches. There is still some question as to whether or not the abdominal approach offers the same opportunity of accomplishing complete bilateral vagus neurectomy which is offered by the transthoracic route.

The literature adequately presents the experimental and clinical data which have led to the present acceptance of this procedure as an important new treatment of peptic ulcer by many of the nation's leading surgeons. The technique of the operation, reports of the immediate results following the procedure and interpretations of the possible physiologic mechanisms involved are to be found in the literature but it is worthy of note that there is a decided scarcity of material on anatomic descriptions of the vagus nerves and their branches between the levels of the main stem bronchi and the diaphragm. Few have pointed out the rather striking variations of the vagus nerves in the immediate supradiaphragmatic levels. That these variations do occur is a definite fact and that they may be of sufficient magnitude to cause failure in accomplishing complete vagotomies in some cases must be recognized. Dragstedt has pointed out the importance of sectioning the vagi immediately above the diaphragm when transthoracic approach is used and has mentioned the necessity of dividing all of the fibers coursing to the stomach. He has further pointed out the fact that anatomic variations are to be found in some cases. After our work was well under way we learned that Edwin M. Miller* in discussing a paper presented by Stoier and associates† at a meeting of the Central Surgical Association in February, 1946, stated that great variations in the distribution of the branches of the vagus nerves at the supradiaphragmatic levels were found in dissections of a number of cadavers and he presented lantern slides illustrating some of the anatomic variations which he had observed. Some weeks prior to the completion of our work we received word of the presentation of a paper entitled "Anatomic Distribution of the Vagus Nerves at the Lower End of the Esophagus in Relation to Gastric Neurectomy for Ulcers." It was presented by Waltman, Walters at a meeting of the Western Surgical Association in December, 1946, and represented the work of Walters, Bradley, Small and Wilson*. The work has not as yet been published and we do not know the details of their observations but from word received they found distinct variations in the distribution of the vagus nerves at the supradiaphragmatic levels and in some cases they were sufficiently variable to be of considerable clinical significance.

Anatomic descriptions of the course of the vagus nerves are to be found in standard anatomy texts but these descriptions lack minute and accurate de-

* (Since the completion of this paper two articles have appeared in the JAMA, 133: 450-461, 1947. One entitled "An Anatomic Study of the Vagus Nerve," by Edwin M. Miller and Carl H. Davis, represents the work reported by Miller at a meeting of the Central Surgical Association in February, 1946. The other entitled "Anatomic Considerations of Gastric Neurectomy," by William F. Bradley, John T. Small, James W. Wilson, and Walman Walters, apparently represents the work reported by Walters at a meeting of the Western Surgical Association in December, 1946. The latter authors have made somewhat different interpretations of their dissected material than we have made from our material.

and reported lower average acid curves than those on which partial gastrectomy alone was performed. Weinstein and associates¹⁰ studied the behavior of three types of gastric pouches in dogs: the Heidenhain pouch with no vagus innervation, the Pavlov pouch with only a small percentage of the vagus fibers intact and a vagal pouch in which practically all vagus fibers were unsevered. Their experiments showed essentially the same acidity curves for all types of pouches in response to the ingestion of food, but when a stimulus was used which operated through the central nervous system, the innervated pouches responded with acidity curves which were high while the noninnervated Heidenhain pouch did not respond at all. Weinstein and his co-workers pointed out the importance of complete vagotomy, recommended transthoracic approach rather than abdominal and stressed the great technical difficulty of performing a complete vagotomy.

Since 1943 when Dragstedt and Owens¹¹ reported improvement in three cases of peptic ulcer following bilateral supradiaphragmatic vagotomies, there has been a steady increase in the numbers of patients on whom this operation has been performed with good immediate results. This fact is distinctly evident from the reports of Dragstedt and his co-workers at the University of Chicago and from the reports of Grimson, Moore and others.¹²⁻¹⁴ Although it is generally agreed that the procedure is not the final answer to the treatment of peptic ulcer, the results are decidedly encouraging and the operation is obviously useful in many selected cases, particularly young patients with no serious stenosis, hemorrhage, hypermotility or hypersecretion and in those who have been resistant to medical treatment. Postoperative complications have been rarely reported although the gastric atony which follows vagotomy in some cases must yet be fully evaluated. In the vast majority of the cases there has been early decrease in the volume and acidity of the gastric secretions, a decrease in the gastric motility and a prompt and dramatic relief of ulcer pain following vagotomy.

The operation as it is generally performed today is essentially the same in most hands. By a transthoracic approach through the bed of the left eighth or ninth rib, the pleura over the posterior mediastinum is incised, the supradiaphragmatic portion of the esophagus mobilized and the anterior and posterior vagus nerves immediately above the level of the diaphragm are located, mobilized and divided. A segment of the proximal portions of each of the nerves is removed and the remaining proximal ends are sutured to the posterior pleura outside of their normal pathways to exclude the possibility of early regeneration. The technique described by Grimson and associates¹³ is to dissect the nerve trunks for a distance of about 10 or 12 cm. above the diaphragm and at this level ligate and divide them. Traction is then put on the distal segments and the nerves are tied and divided at the level of the diaphragm, the tied ends retracting below the diaphragm. It is thought that the defect in the vagus nerves lessens or prevents late functional nerve regeneration without transplanting the nerves as has been suggested by Dragstedt, Moore and his co-workers.¹² Opening the diaphragm and resected a portion of each nerve from

just below the lung root to the mid portion of the gastric fundus. Transthoracic vagotomy is at present being used more widely than the transabdominal approach although Dragstedt and his co-workers have had wide experience with both approaches. There is still some question as to whether or not the abdominal approach offers the same opportunity of accomplishing complete bilateral vagus neurectomy which is offered by the transthoracic route.

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trunks of the nerves at the levels just mentioned. Baptista²² presented an excellent and detailed description of dissections of the vagi in vertebrates in which cats were the mammalian representatives. The course of the vagus nerves from the hilar level to the stomach which we herewith present is based on text material,²³⁻²⁵ Baptista's findings, and our own observations (Fig. 6). The vagi pass caudad as single trunks along either side of the trachea then dorsal to the main stem bronchi at which level they give off pleuropulmonary, tracheobronchial and vascular fibers. The respective nerve trunks then course medially to either anterolateral aspect of the esophagus and at the level immediately below the hiatus each nerve divides into anterior and posterior branches, the anterior branches of each nerve joining to form the anterior esophageal plexus and the posterior branches joining to form the posterior esophageal plexus. As a general rule it may be said that the major part of the anterior esophageal plexus consists of fibers from the left nerve and the major part of the posterior plexus consists of fibers from the right nerve. Numerous fibers are given off from both anterior and posterior plexuses which enter the esophagus and we observed many fibers derived from the anterior plexus which entered the pericardium at various levels. In addition to the pericardial and esophageal branches the plexuses also give off pleuropulmonary and vascular fibers. In the descriptions of the course and general character of the nerves at these levels which we have found, the gastric divisions of the vagi are reported as single trunks, one the left or anterior nerve and the other the right or posterior nerve. The anterior nerve is described as coursing along the antero-left lateral aspect and the posterior nerve along the postero-right lateral aspect of the lower esophagus to the diaphragm at which level they pass through the hiatus and are distributed to the stomach, the anterior supplying the anterior aspect and the posterior nerve supplying the posterior aspect of the stomach. In contradistinction to this we found rather marked variations in the anatomic appearance of the gastric divisions of the vagi in many cases, details of which will appear elsewhere in this presentation. We found that there are in all cases an anterior or left nerve trunk or nerve complex and a posterior or right nerve trunk or nerve complex formed respectively from the anterior and posterior esophageal plexuses. The anterior courses along the esophagus on its antero-left lateral aspect, the nerve or nerves varying in location in most cases from the anterior midline to a point just medial to the true left lateral position and the posterior courses along the right postero-lateral aspect of the esophagus, varying in location in most cases from the posterior midline to a point just medial and posterior to the true right lateral position. The anterior and posterior nerves or complexes then pass through the hiatus and divide into branches, some of which supply respectively the proximal portions of the anterior and posterior aspects of the stomach and some of which course to the proximal part of the lesser curvature where they anastomose and continue distally along the lesser curvature, many of the fibers coursing within the fat and fascia of the gastroduodenal ligament. From here fibers are given off at regular intervals which course downward more or less at right angles to the lesser curvature and supply the anterior and

posterior portions of the stomach. The distribution of the vagus fibers to the stomach as described here is of importance in that it explains for the most part the early failures in accomplishing complete vagus sections. It was previously thought that the anterior and posterior gastric nerves were distributed over the gastric walls and the fact that the nerves course through the gastrohepatic ligament at the lesser curvature and along this course give off branches to the anterior and posterior gastric surfaces was not taken into account. Because of this fact the early transabdominal vagotomies were incomplete inasmuch as complete vagal continuity was not interrupted the fibers coursing through the gastrohepatic ligament having been left intact. This point has recently been mentioned by Dragstedt** and our dissections substantiate his observations.

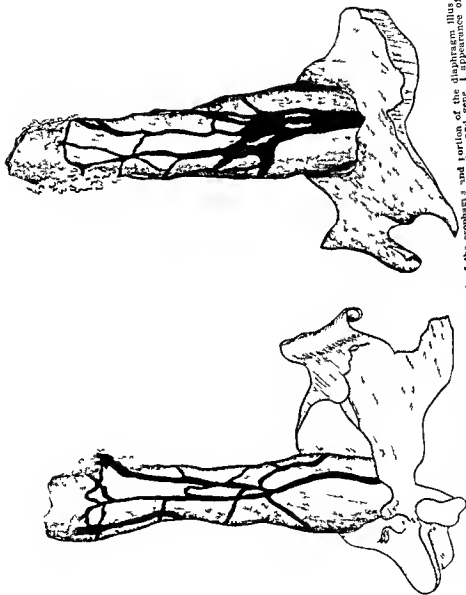
For the study and analysis herewith presented fifty esophagi* were removed at necropsy the specimens including the lower trachea main stem bronchi and a portion or all of the stomach in as many cases as was possible. A few specimens obtained early in the course of the work were studied and dissected in the fresh state but it was later considered advisable to complete the studies on fixed specimens inasmuch as more accurate evaluation of all fibers could thereby be made. The ages of patients from which specimens were removed ranged from 2 to 80 years and the ratio of males to females was approximately equal. Body sizes were of course variably represented and there was no apparent relationship between body sizes and the sizes and character of the nerves. The course of the vagi from the level of the primary bronchi to the stomach was studied general structure of the so called esophageal plexuses was noted and the general relationship of the nerves to the stomach was examined in a number of specimens but special emphasis was placed on the study of variations in appearance formation and distribution of the gastric divisions of the vagi which form from the anterior and posterior esophageal plexuses and course to the stomach through the esophageal hiatus.

For purposes of simplification a classification was decided upon which would enable us to place the specimens studied into classes based on certain major anatomic variations of the gastric divisions of the vagus nerves at the supradiaphragmatic levels. The classification is as follows:

I *Simple or basic pattern* in which a single primary trunk forms from the anterior and posterior esophageal plexuses forming thereby the so-called left or anterior and the right or posterior nerves and entering the hiatus as single trunks. The classification of the specimens is based on the general character of the nerve or nerve complex between the levels of the esophageal plexus and the upper level of the diaphragm (Figs 1 2 and 3).

II *Intermediate pattern* in which a single primary trunk forms from the anterior and/or the posterior esophageal plexus or plexuses but divides into two or more secondary nerve trunks before entering the hiatus in their course to the stomach (Figs 4 and 5).

*We should like to express our appreciation of the cooperation of the Medical Examiner's Office, New York N. Y. for having furnished us with the majority of the specimens studied.



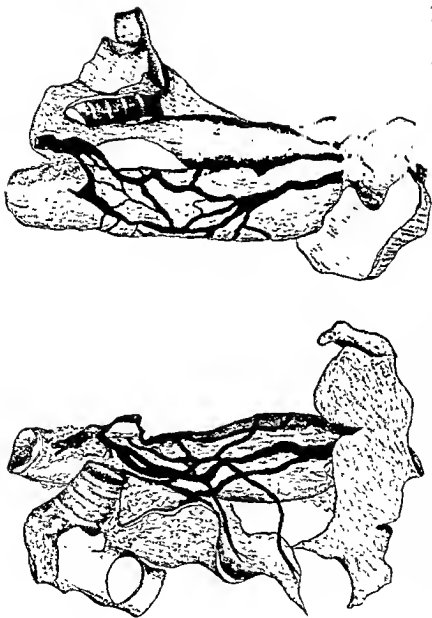


Fig. 1.—Dissected specimen illustrating anterior (left) and posterior (right) views of the esophagus with attached trachea, bronchi, and aorta. The branching of the esophageal arteries and veins is shown in black. This specimen provides anterior and posterior examples of the double pattern in which a single nerve trunk forms from the esophageal plexus and enters the esophageal hiatus.

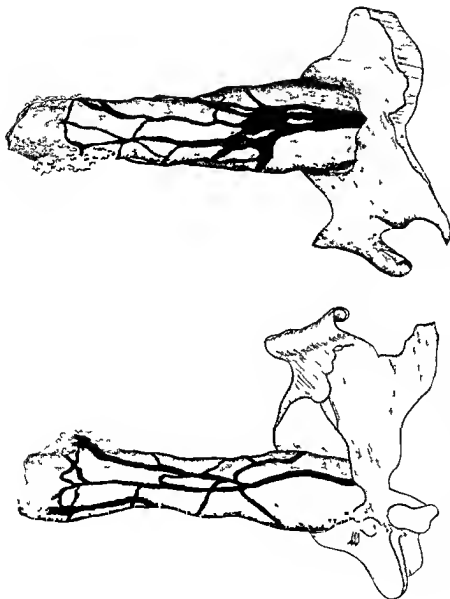


Fig. 2.—Anterior view (left) and posterior view (right) of the diaphragm and portion of the esophagus illustrating another aspect of the same pattern. Note the marked difference in the size and general appearance of the anterior or left and the posterior or right gastric nerves.

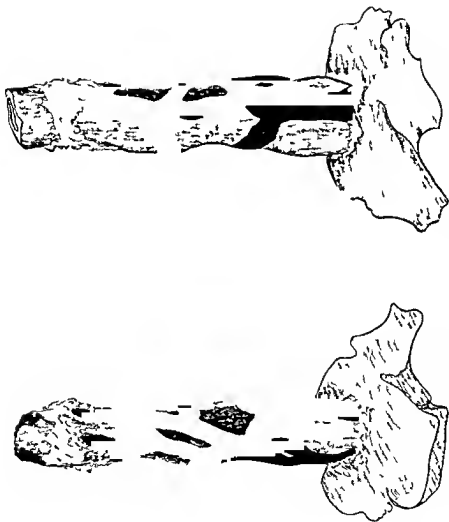


Fig. 3—Right internal view, (left) and anterior view of the stomach and duodenum, showing the pyloric region and the duodenum. The pyloric region is shown in the upper part of the illustration, and the duodenum is shown in the lower part. The pyloric region is shown in the upper part of the illustration, and the duodenum is shown in the lower part.



Fig. 4.—Three specimens, an anterior view (left) and posterior view (center and right), illustrating slight variations of the intermediate pattern, in which a single trunk forms from the esophageal plexus and divides into secondary divisions before entering hiatus. Note, in two of the specimens the distribution of the nerves within the hiatus and below the diaphragm.

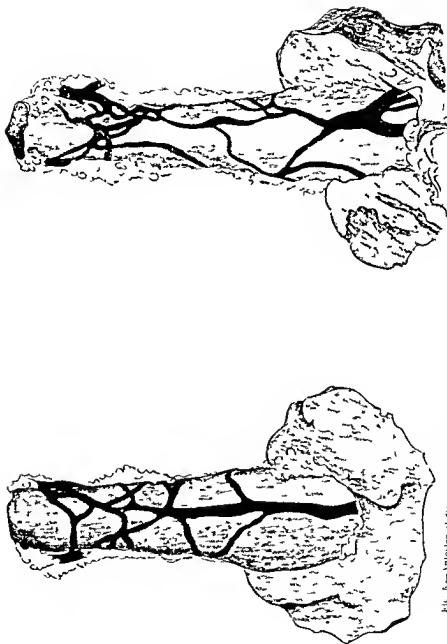


Fig. 5.—Anterior (left) and posterior (right) aspects of a specimen illustrating an internal iliac system. In the internal iliac system the internal iliac artery and vein are shown entering the pelvis at the level of the iliac crest.

III Complex pattern, in which two or more primary trunks form from the anterior and/or the posterior esophageal plexus or plexuses before entering the esophageal hiatus in their course to the stomach regardless of the number or character of the secondary nerve trunks (Figs 6 to 10)

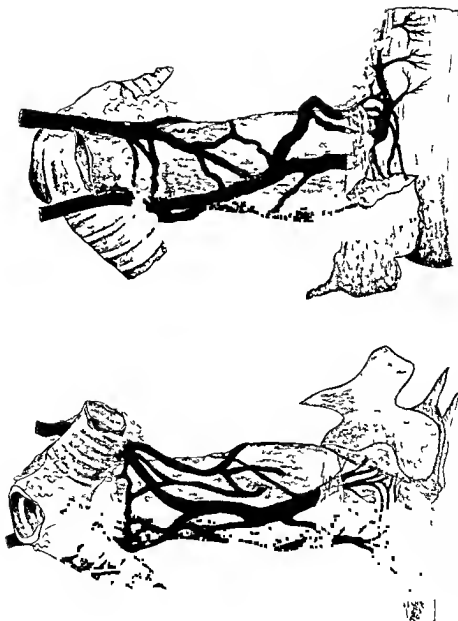
In placing the specimen in any part of the classification, inasmuch as the anterior and posterior nerve complexes may differ in class, the classification is made on the basis of the more complicated of the two nerve complexes

Table I shows the classifications into which the various specimens were placed, the number and percentage of specimens which had anterior and posterior nerve trunks or nerve complexes of the same type, the number and percentage of nerves at the immediately supradiaphragmatic levels which were in 'normal' positions, those which were found in "abnormal" positions and those

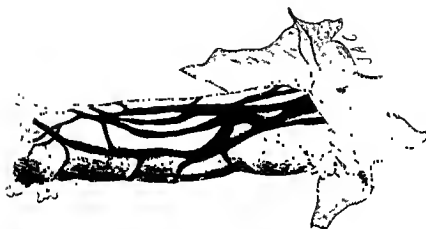
TABLE I

	NUMBER	PER CENT
Classification of specimens		
Pattern I (Simple)	30	60
Pattern II (Intermediate)	8	16
Pattern III (Complex)	12	24
Specimens having anterior and posterior nerves or nerve complexes of the same pattern		
Pattern I	30	60
Pattern II	0	0
Pattern III	2	4
Locations of the gastric nerves or nerve complexes		
Anterior (left) nerve or complex		
Normal position*	44	88
Abnormal position*	6	12
Complexes one fiber of which is out of the normal position	0	0
Posterior (right) nerve or complex		
Normal position	41	82
Abnormal position	9	18
Complexes one fiber of which is out of the normal position	2	
Gross morphology of nerve trunks immediately above diaphragm		
Oval	92	73
Flat	34	27
Round	0	0
Widths of nerve fibers at upper level of diaphragm		
0.1 to 0.15 cm	1*	10.3
0.2 to 0.25 cm	33	26.1
0.3 to 0.35 cm	3*	26.1
0.4 to 0.45 cm	20	16.0
0.5 to 0.6 cm	22	17.5
0.8 to 0.9 cm	5	4.0
Degree of prominence of nerve fibers below the esophageal plexuses		
Prominent	88	70
Moderately prominent	21	16
Obscure	17	14
Levels of the lower limits of the anterior and posterior esophageal plexuses measured from the upper level of the diaphragm		
Under 1.0 cm	5	5
1.0 to 2.0 cm	33	32
2.0 to 3.0 cm	36	29
3.0 to 4.0 cm	17	17
4.0 to 5.0 cm	5	5
5.0 to 6.0 cm	3	3
6.0 to 6.5 cm	1	1

*for explanation of terms normal and abnormal positions see text.



The larynx is the organ of voice, and is situated in the neck. It is composed of cartilages, muscles, and ligaments. The thyroid cartilage is the largest and most prominent. The cricoid cartilage is situated below the thyroid. The epiglottis is a leaf-shaped cartilage that prevents food from entering the trachea. The vocal folds are located within the larynx and are responsible for the production of sound. The trachea is the windpipe, which carries air from the lungs to the larynx.



t) and posterior view (right) of a specimen illustrating very complex and posterior (right) nerves. An example of pattering which



Fig. plexus might be

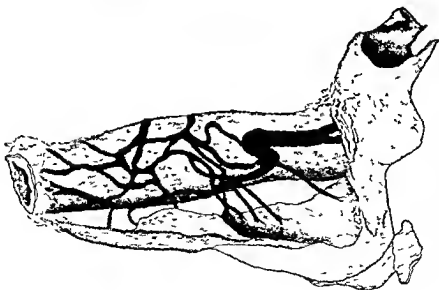
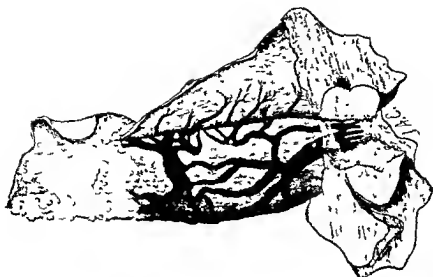


Fig. 9—Anterior view (left) and posterior view (right) of a specimen with attached arterial trunk in posterior view. The arterial trunk is the one which supplies the esophagus. The other vessels are branches of the latter within the field of view.

which presented fibers of the nerve complexes which were in 'abnormal' positions. The table also indicates the number and percentage of nerve fibers which presented certain morphologic characteristics the numbers and percentages of nerve fibers which were in various ranges in regard to their width at the upper level of the diaphragm the numbers of the fibers which were prominent moderately prominent or obscure in appearance and to palpation. Finally, it presents figures indicating at what levels above the diaphragm the anterior and posterior esophageal plexuses terminate and form the gastric divisions of the vagus nerves.

From the analysis of the material it can be concluded that a distinct majority of the gastric divisions of the vagi are of a simple pattern with a single trunk representing the left or anterior nerve and a single trunk representing the right or posterior nerve. In our series thirty specimens or 60 per cent were placed in this classification. Relatively few specimens fell into the intermediate classification. Eight specimens or 16 per cent were of this pattern in which single trunks were formed from the anterior and/or the posterior esophageal plexuses but presented two or more secondary trunks which formed from the primary trunk before entering the esophageal hiatus. Twelve or 24 per cent of the specimens were of the complex pattern in which there was more than one primary trunk formed from the anterior and/or the posterior esophageal plexuses. These figures suggest that a distinct majority of the cases encountered should present single gastric nerves which lack an immediately supradiaphragmatic complex and consequently present no technical difficulty in accomplishing a complete bilateral vagus neurectomy. The few intermediate types which one encounters should involve somewhat greater technical difficulty in that the operator should attempt to locate the primary trunk of the complex and division should be made at this point. If this is not done and division is attempted above or below this level one becomes involved in the fibers which make up a part of the complex esophageal plexus or in the multiple secondary trunks which enter the hiatus. One is thus confronted with the potential danger of incomplete division of all of the fibers coursing to the stomach. Inasmuch as this pattern does not occur in great numbers and since with care in choosing the proper level for division complete neurectomy should be accomplished one need have little fear of operative failure. However recognition of the fact that this pattern does occasionally occur is important. The fact that twelve or 24 per cent of the specimens were of the complex pattern should be taken seriously a knowledge of these anatomic variations is essential and the clinical importance of the occurrence of these multiple primary trunk patterns should be recognized.

From Table I it may be noted that except for the specimens which were placed in the simple or basic group the anterior and posterior nerves which are naturally of the same type most cases encountered would present anterior and posterior nerve complexes which differ in pattern. Only two specimens of the intermediate and complex groups presented complexes of the same type.

As has been previously indicated the most common location of the gastric nerves or nerve complexes has been found to be within an area just above the

diaphragm between the anterior midline and a point just anterior and medial to the true left lateral position for the left nerve, and between the posterior midline and a point just posterior and medial to the true right lateral position for the right nerve. These positions we have designated as normal and fibers of the gastric divisions of the vagi which have been found located outside of these arcs we have designated abnormal in position. Of the anterior nerves or nerve complex examined forty-four or 86 per cent were found in the so called normal position and only six or 12 per cent of the specimens were in abnormal positions. Of the posterior nerves or nerve complexes forty-one, or 82 per cent were in normal position, and nine or 18 per cent were in abnormal positions. Of the posterior nerves three specimens presented com

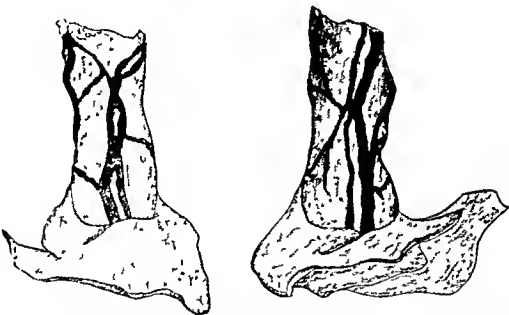


Fig. 9 — Anterior (left) and posterior (right) aspects of a specimen illustrating another variety of the complex pattern. Two primary trunks for the posterior esophageal plexus.

plexes which were in normal position but each with a single fiber which was in an abnormal position. It is gratifying to note that the anterior and posterior gastric nerves usually are found within fairly limited arcs. However since there are occasional variations in their locations and since there are rather marked differences in the sizes of the nerves some of which are quite obscure one must recognize the fact that some fibers may be overlooked at the time of vagotomy and an incomplete division result.

As far as the gross morphology of the nerve fibers is concerned ninety-two or 73 per cent were oval in shape and thirty-four or 27 per cent were flat or ribbonlike. None of the nerves appeared as round fibers. Many of the flat fibers would be difficult to palpate and a few of these would be difficult to see

at operation as is indicated later in the discussion of the number and percentage of obscure fibers noted in the series

From the figures indicating the widths of fibers at the upper level of the diaphragm it may be seen that 52.3 per cent of the fibers were from 0.2 to 0.35 cm. and 33.5 per cent were relatively large ranging from 0.4 to 0.6 cm. in width. Only 10.3 per cent were under 0.15 cm. and 3.9 per cent were over 0.8 cm. in width.

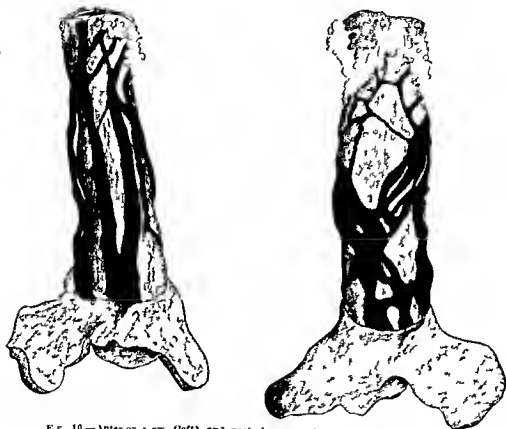


FIG. 10—Anterior view (left) and posterior view (right) illustrating another variety of the complex pattern. Note the unusually complex posterior nerve pattern and the remarkably large nerve fibers.

Of the fibers examined eighty-eight or 70 per cent were considered distinctly prominent and should have been easily palpated and visualized at operation. Twenty-one or 16 per cent were moderately prominent but should have been easily demonstrable. Seventeen or 14 per cent were considered obscure and would have had to be sought for meticulously at the time of vagotomy.

The level of the lower limits of the anterior and posterior esophageal plexuses varied from 0.2 to 6.5 cm. above the upper level of the diaphragm. 69 per cent were from 1.0 to 3.0 cm., 17 per cent from 3.0 to 4.0 cm., and only 9 per cent were at higher levels from 4.0 to 6.5 cm. It is important to have some idea

diaphragm between the anterior midline and a point just anterior and medial to the true left lateral position for the left nerve and between the posterior midline and a point just posterior and medial to the true right lateral position for the right nerve. These positions we have designated as normal and fibers of the posterior divisions of the V-L-1 which have been found located outside of these areas we have designated abnormal in position. Of the anterior nerves or nerve complexes examined forty-four, or 88 per cent were found in the so-called normal position and only six or 12 per cent of the specimens were in abnormal positions. Of the posterior nerves or nerve complexes forty-one or 82 per cent were in normal position and nine or 18 per cent were in abnormal positions. Of the posterior nerves, three specimens presented com-



at operation as is indicated later in the discussion of the number and percentage of obscure fibers noted in the series

From the figures indicating the widths of fibers at the upper level of the diaphragm it may be seen that 52.3 per cent of the fibers were from 0.2 to 0.35 cm and 33.5 per cent were relatively large ranging from 0.4 to 0.6 cm in width. Only 10.3 per cent were under 0.15 cm and 3.9 per cent were over 0.8 cm in width.

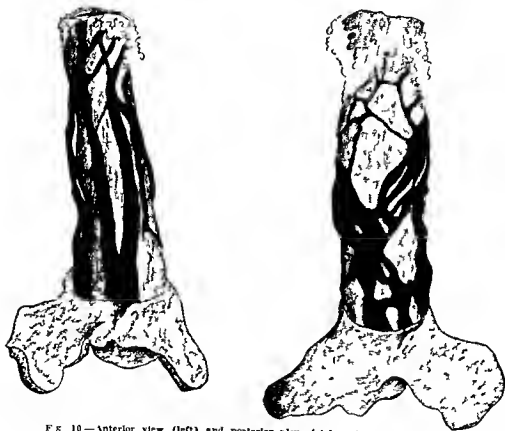


FIG. 10—Anterior view (left) and posterior view (right) illustrating another variety of the complex pattern. Note the unusually complex posterior nerve pattern and the remarkably large nerve fibers.

Of the fibers examined eighty-eight or 70 per cent were considered distinctly prominent and should have been easily palpated and visualized at operation; twenty-one or 16 per cent were moderately prominent but should have been easily demonstrable. Seventeen or 14 per cent were considered obscure and would have had to be sought for meticulously at the time of vagotomy.

The level of the lower limits of the anterior and posterior esophageal plexuses varied from 0.2 to 6.5 cm above the upper level of the diaphragm. 69 per cent were from 1.0 to 3.0 cm, 17 per cent from 3.0 to 4.0 cm, and only 9 per cent were at higher levels from 4.0 to 6.5 cm. It is important to have some idea

SURGERY IN RADIATION INJURY OF THE STOMACH

RALPH F BOWERS, M D,* AND IRVING B BRICK, M D,† WASHINGTON, D C

INTRODUCTION

IN A previous report¹ on radiation effects on the human stomach, it was pointed out that very little is known relative to the effects of radiation on the human stomach. In the few human cases that have been reported^{2, 3} in the literature concerning radiation injury to the stomach, the radiation injury occurred in stomach infiltrated with tumor where destruction of the tumor tissue was primarily responsible. In these cases, ulcer and perforation were reported following radiation. However, little can be learned about the clinical course and the laboratory studies in these patients who had radiation lesions of the stomach. The complicating factor of the pathologic lesions existing in the stomach prior to receiving radiation does not lend itself easily to an analogy with the experimental animal studies.

Various animals have been used to demonstrate the effect of radiation on the stomach. Engelstad⁴ found distinct changes in the stomachs of rabbits after roentgen irradiation. A dose of 1,500 r or more regularly produced ulcerations in the stomach coming on in the second to fourth week after radiation. Perforation was noted to have occurred frequently and in a few cases considerable hemorrhage from the ulcers was noted. If the animals lived more than two to three months after radiation, the ulcer showed a tendency toward healing and epithelization. Hueper and DeCarvajal Porero⁵ administered radiation in doses of 300 r up to a total of 6,000 r to the stomach of dogs and within four weeks produced marked loss in body weight, a moderate to severe anemia and perforating gastric ulcers. Another series of dogs that received a total of 4,875 r over a twenty five week period did not reveal any abnormal significant gross and histologic changes of the internal organs.

We have been able to observe cases of massive irradiation to the epigastric area in patients in whom there was no gastric pathology or history of previous gastrointestinal disease. All these patients were receiving radiation for metastatic retroperitoneal lymph nodes from testicular tumors or for prophylactic treatment of the retroperitoneal lymph nodes which are the first in the chain of metastasis from testicular tumor. All these patients had no previous history or symptomatology that could be remotely connected with the stomach and the results obtained in the treatment of their primary diseases have afforded coincidentally, a human analogy to and confirmation of the experimental animal work on the irradiation of stomachs.

MATERIAL

As pointed out in a previous paper,¹ complications that required surgery were noted in two cases. Since that time four other patients have had gastric surgery and in this paper we are presenting this series of cases. In Table I is

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*Formerly Chief Surgical Service Walter Reed General Hospital

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listed an outline of the data in this series. Specimens obtained at operation in these necessary surgical procedures have added a great deal of information to the pathologic studies of these stomachs. Surgery in cases of a similar nature has not been previously reported elsewhere.

TABLE I

PATIENT	DOSAGE IN R AT LEVEL OF D ₅ AND DAYS TO COMPLETE	PARTIAL GASTRECTOMY DONE DAYS AFTER COMPLETION OF RADIATION	OPERATIVE FINDINGS
1 C	6,450 r in 52 days	95	Perforation of a 3 cm ulcer on posterior wall of antrum (Fig 1)
2 Tr	5,880 r in 44 days	169	Thickened mucosa submucosal ecchymosis, and generalized petechial hemorrhages of gastric mucosa (Fig 2)
3 H	5,304 r in 55 days	157	Ulcer 2 cm in diameter and 2 mm deep proximal to the pyloric ring found. Mucosa contained petechial hemorrhages (Fig 3)
4 Y	4,105 r in 49 days	190	Perforated ulcer 2 cm in diameter found on the posterior antral wall (Fig 4)
5 B	5,090 r in 54 days	189	On the posterior wall and involving the pyloric ring a sharply demarcated ulcer 1½ cm in diameter was found (Fig 5)
6 Ty	4,800 r in 53 days	125	Peritonitis resulting from subacute perforation with abscess formation of a 3 by 3 by 2 cm irregularly triangular ulcer in the antrum

In the first three cases reported, surgery was done as a life saving measure in the treatment of gastric hemorrhage which occurred as a complication of radiation injury. The first case led us to the awareness that such a complication could occur since no previous similar case has been reported in the literature. With this awareness in mind, careful observation of other patients who had gastric radiation injury led to more prompt surgery in the second and third cases. In the last three cases reported, the indication was intractable pain which had not been alleviated by a rather lengthy trial of a rigid medical regime, similar to that for peptic ulcer. Unfortunately several of these patients had other complications which were noted at the time of operation particularly small intestinal radiation injury. We now have several cases which have shown ulceration by x-ray and gastroscopically and which have been treated on a medical regime with alleviation of symptoms and a betterment of the general condition which has led us to select only the most severe cases for surgery. The apparent progressiveness of the symptoms and the pathologic condition of the stomachs has led us to the belief that some of these patients may eventually require gastric surgery.

Intensive study of the radiation doses and the tolerance of the stomach and other organs of the gastrointestinal tract in human beings is now in the process of completion*. In the series that is being followed here there is apparently a

*This is being carried on mainly by Lieutenant Colonel Milton Friedman, Chief Radiation Therapy Section, Walter Reed General Hospital.

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We have been able to observe cases of massive irradiation to the epigastric area in patients in whom there was no gastric pathology or history of previous gastrointestinal disease. All these patients were receiving radiation for metastatic retroperitoneal lymph nodes from testicular tumors or for prophylactic treatment of the retroperitoneal lymph nodes which are the first in the chain of metastasis from testicular tumor. All these patients had no previous history or symptomatology that could be remotely connected with the stomach and the results obtained in the treatment of their primary diseases have afforded coincidentally, a human analogy to and confirmation of the experimental animal work on the irradiation of stomachs.

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TABLE I

PATIENT	DOSE IN R AT LEVEL OF D AND DAYS TO COMPLETE	PARTIAL GASTRECTOMY DONE DAYS AFTER COMPLETE RADIATION	OPERATIVE FINDINGS
1 C	6456 r in 39 days	95	Incision of a 3 cm ulcer on posterior wall of antrum (Fig 1)
2 Tr	5890 r in 44 days	169	Thickened mucosa, submucosal edema and generalized petechial hemorrhages of gastric mucosa (Fig 2)
3 H	5304 r in 55 days	154	Ulcer 2 cm in diameter and 2 mm deep proximal to the pyloric ring found. Mucosa contained petechial hemorrhages (Fig 3)
4 I	6100 r in 49 days	190	Perforated ulcer 2 cm in diameter found on the posterior antral wall (Fig 4)
5 B	5096 r in 54 days	199	On the posterior wall and involving the pyloric ring a sharply demarcated ulcer 1½ cm in diameter was found (Fig 5)
6 Ty	4800 r in 53 days	94	Peritonitis resulting from subacute perforation with abscess formation of a 2 by 3 by 2 cm irregularly fungoid ulcer in the antrum

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very marked individual variation in tolerance to radiation. Quite a few patients who have received 5,000 r or above to the epigastric region at the level of the eleventh dorsal vertebra have had no gastrointestinal symptoms. On the other hand, ulceration has been noted in patients with much less radiation. The roentgen formula used in these cases was 1000 kilovolts, 3 milliamperes, filter 3 mm tungsten, and a focal skin distance of 70 or 100 cm, 88 to 40 r respectively, being delivered per minute.

CASE REPORTS

CASE 1—C was 21 years old. In March 1945, he dropped an oil cooler out of an airplane and in trying to get out of the way, he noted pain in his left side and left testicle. At the time, he felt as if someone had kicked him there and about one week later he noted that the testicle was becoming hard and enlarged. Because of the enlargement of the left testicle, the patient was hospitalized and applications of ice packs were given. There seemed to be a slight diminution in the size of the testicle and in July, 1945, he returned to duty. However, the testicle continued to become enlarged, although no further pain was noted. He was again admitted to the hospital and after aspiration of the testis with negative laboratory results, he was transferred to Walter Reed General Hospital. Intravenous pyelograms and x-ray studies of the chest and pelvis were negative. The patient received ten x-ray treatments from October 2 to October 15 for a total tumor dose of 1000 r. It was estimated that there was about 20 per cent reduction in size and that the testicle felt softer than it had prior to radiation. On Oct. 18, 1945, radical orchiectomy with resection of the retroperitoneal nodes was done. A number of small nodes were removed from the external iliac and lower portion of the aorta. There was a large fixed ovoid mass 10 cm long, 5 cm wide, and 3 cm deep plastered against the aorta in the midline and fixed to the anterior surface of the vertebral column. The lower border of this mass was at the level of the lower pole of the left kidney and extended proximally for a distance of 10 cm. At the same time the testicle and spermatic cord were removed. Histologic study of the testicle revealed a teratoma with embryonal adenocarcinoma component, the latter showing moderate to marked radiation effect. The large para-aortic nodes were believed to be metastatic. Irradiation was started and the patient received twenty-four x-ray treatments from Oct. 17 to Nov. 29, 1945. A tumor dose of 6406 r in thirty-two days was delivered over the left umbilical and dorsolumbar portals. As a result of this intensive radiation only a moderate first degree skin erythema was noted. Very little radiation sickness was experienced during this period. The patient was granted a thirty-day furlough following completion of irradiation.

He was readmitted to the hospital Jan. 4, 1946. He stated that about two weeks previously, in the middle of December after leaving the hospital, he experienced pain in the lower epigastrium, radiating to the back. Slight relief was noted after drinking ginger ale and orange juice. At night the pain was intermittent and rather sharp. No relationship to meals was noted. No melena or hematemesis had been noted. With the attacks of pain there was vomiting. Physical examination was not remarkable. Because of the continuance of the abdominal pain a gastrointestinal series was obtained and this showed the prepyloric region of the stomach to be constricted and funnel shaped with partially fixed walls. The rugae in this area were enormously enlarged. In the prepyloric region near the pyloric valve a large ulcer was thought to be present. The duodenum appeared normal. At this time the patient was transferred to the gastrointestinal service and was placed on a bland diet, amylase, tincture of belladonna, and phenobarbital. The patient seemed to improve for the first two weeks, although sporadic pains were noted in the lower abdomen. There was no vomiting during the first several weeks on an ulcer regime, but the patient's appetite was very poor and he still felt very weak. Fractional gastric analysis with histamine revealed specimens containing 0, 1, 115, 100, and 65 units of free hydrochloric acid. In the last week of February the patient started vomiting at least once a day usually in the afternoon. The

pain that had been described continued. On Feb 25, 1946, the patient vomited approximately 750 cc of bloody material and was given a transfusion because of impending shock. The patient was placed on routine therapy for gastrointestinal hemorrhage with a modified Meulen graht diet and was comfortable until March 1, 1946, at which time he vomited over 1,000 cc of bloody material. Blood pressure immediately thereafter was 60/30 and a transfusion with 500 cc of blood, which had been kept available on the ward, was immediately given. Another sublethal episode of vomiting occurred ten hours later, necessitating another transfusion. From this time forward, the patient was vomiting blood daily, necessitating daily transfusions of 500 to 1,000 cc of whole blood. The situation appeared hopeless and it was agreed that the only possibility of preventing death from hemorrhage was by surgery. Two hours prior to operation of March 5 the patient vomited about 1,000 cc of blood and with the transfusion continuing as he was brought to the operating room laparotomy was performed.

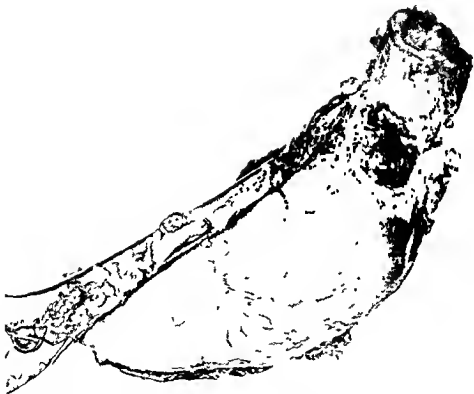


Fig. 1 (Case 1) — Perforation of an ulcer 4 cm in diameter on the posterior wall of the stomach.

Palpation of the abdominal wall revealed no undue fibrosis or thickening and no edema or fibrosis of the subcutaneous tissues, fascia, and rectus muscle was noted. After opening the peritoneum a fibrotic appearing vascular pylorus was noted. An ulcer about the size of a quarter on the posterior wall of the antral region was noted to have perforated (Fig 1). In the region of the perforation there was a considerable amount of fibrosis and edema. In the bottom of the pit made by the perforation of the ulcer, there was a large vein which

bled copiously when touched. This was believed to be a branch of the mid-colic vein and after being transfixed, bleeding ceased immediately. The duodenum was cut across about one and one-half inches below the pyloric vein and closed. A gastrojejunostomy was done and an anastomosis was completed. Examination of the transverse colon and other structures lying within the path of irradiation disclosed no evidence of radiation injury to those structures, with the possible exception of one loop of the jejunum which seemed to be somewhat thickened. Palpation of the retroperitoneal area at the site of the node which was noted at the time of the radical dissection of retroperitoneal nodes revealed no evidence of disease. The patient tolerated the operation very well. Whereas he entered the operating room practically in shock, he left it with a blood pressure of 120/70 and a pulse rate of 72.

The postoperative course was very smooth and the patient was eating a soft diet six days after operation. He was on a full ambulatory status three weeks after the operation. At the time of operation, the patient weighed 96 pounds and in the first month postoperatively gained sixteen pounds. There was alleviation of all the patient's symptoms and after six weeks he was able to tolerate a regular diet. The only difficulty occurred from slight drainage from the abdominal wound which continued for several months. Except for the small incisional draining sinus which revealed, on July 5, 1946, suture material, the patient has had no difficulty whatever. At the time of reporting, Aug. 31, 1946, some five months postoperatively, the patient weighed 130 pounds and had no gastrointestinal symptoms. Throughout, monthly chest roentgenograms were taken and have been reported negative. A fractional gastric analysis with histamine done April 13, 1946, more than one month after the operation, showed no free hydrochloric acid. Small intestinal study done April 20 showed a satisfactorily functioning gastrojejunostomy and no changes in the small intestine.

At follow up examination one year postoperatively, the patient had no symptoms and was well.

Comment—This patient was one who had a testicular teratoma with embryonal adenocarcinoma component and rather extensive retroperitoneal metastasis on admission to this institution. A tumor dose of 6456 r was delivered in thirty-two days which represents rather massive and thorough irradiation in a comparatively short period of time. Despite this heavy dosage the patient had only a moderate first degree skin erythema and very little radiation sickness, indicating that his tolerance, at least as far as the skin was concerned to radiation was very high. In this case a 10 by 15 cm portal was used. Thirty-two days after completion of radiation therapy gastric symptoms began to appear and there was confirmation of gastric changes by x-ray. A medical regime was not very successful in controlling the patient's symptoms. The weakness, anemia, and lack of appetite that the patient had seemed to be a rather typical triad in addition to the gastrointestinal symptoms that are present in all these patients. It is also interesting in view of the widely prevalent belief that radiation depresses the secretion of hydrochloric acid in the stomach that this patient's gastric analysis with histamine showed several specimens containing over 100 units of free hydrochloric acid. With the onset of hematemesis approximately 2½ months from the onset of the gastrointestinal symptoms a radical departure in the mode of treatment was indicated. In this patient the medical attempt to control bleeding we now agree was too long and because of the repeated episodes of bleeding surgically he was a poor risk. As many authors have indicated, the results of surgery of this type are almost directly correlated with the number of successive attacks of hemorrhage. It was quite fortunate

that at operation the bleeding joint was found quickly and tied off immediately. In this case the examining surgeon did not find radiation changes in other parts of the gastrointestinal tract. Of interest particularly to the radiation therapist is the fact that the previously noted retroperitoneal metastatic lesion had completely disappeared. The postoperative course in this case was so good that it led to an evaluation of our methods in handling future cases.

CASE 2.—A 30-year-old soldier who enjoyed his usual state of health until March 1945. At that time overseas he began to complain of low abdominal pain which he described as crampy and occurring chiefly at night. The pains continued to get worse and there was also constant severe low backache. There were no other gastrointestinal symptoms present. The patient returned to the United States and because of the continuation of symptoms sought medical attention. He was admitted to an Army regional hospital on July 26, 1945. During this period of illness the patient felt he had lost ten pounds in weight. A cervical lymph node was biopsied and the pathological report of papillary adenocarcinoma metastatic to soft organs unknown was returned. Because of this finding he was transferred to Walter Reed General Hospital on September 20, 1945.

On admission to this hospital the patient complained only of low abdominal crampy pain. Small satellite glands were noted in the left axilla. A firm hard mass in the mid abdomen extending about 10 centimeters below the umbilicus and five inches to the left of the midline was noted. The mass was as quiescent. Biopsy lesions were noted to be all anaplastic. X-ray studies revealed a large retroperitoneal mass which displaced the colon and both kidneys. The poles of both kidneys were rotated entirely. A slight degree of gynecomastia was noted one week after admission. From September 28 to October 24, 1945, the patient received thirty x-ray treatments for a total of 3,000 r to the anterior and umbilical portal 300 r to the posterior abdominal portal and 4,000 r to the left side of the neck. Six additional x-ray treatments were given from November 3 to November 10, 1945, for a total dose of 4,000 r to the anterior and posterior umbilical and posterior umbilical portal. This made a total tumor dose at the level of the diaphragm of 8,800 r in forty-four days. This was followed by a routine portal during this period of radiation the patient experienced no notably severe radiation on the skin and no other complications. As a result of the radiation the mass in the abdomen shrank rapidly and the nodes in the neck disappeared completely.

It was the opinion of the tumor board to which this case was presented that the most likely site of origin was testicular. At the completion of radiation therapy the patient was granted a thirty-day furlough. From this he returned on January 5, feeling fairly well. There was no particular loss in weight. He did experience some nausea and occasional vomiting which began about forty-five days after the completion of the therapy. The patient was granted another furlough. After return from this furlough, March 1, 1946, there was noted a small increase in the size of the right testicle. Accordingly on March 5, 1946, a right orchiectomy was done and histologic study revealed a seminoma. Following this operation the patient received 10,000 r in proplastic x-ray treatments from March 15 to April 16, 1946, for a dose of 2,000 r in suprapubic 600 r right anterior and 4,000 r left anterior and 4,000 r right posterior and 4,000 r left posterior and chest. On March 25, 1946, a routine electrocardiogram revealed the presence of a dense oval mass superimposed on the cardiac shadow which appeared to be due to large nodal metastatic nodes that extended into this area from the large retroperitoneal mass. With cessation of the radiation to the chest portal there was disappearance of the chest shadow within two weeks.

The patient's general condition was good until the first week in April 1946. At that time there was the onset of vomiting the vomitus containing clots of blood. At about the same time the patient began to feel weak and had dizzy spells and severe lethargy. The vomiting was not accompanied by nausea or pain and was entirely unrelated to meals. The patient did not feel that food precipitated the vomiting. An upper gastrointestinal x-ray series on April 6, 1946, revealed no retention of food in the stomach. Tenderness



Fig. (Case 2) — (1) Tumor of the entire ilio-lumbar region

over the antrum with narrowing of the stomach in this area, and hypertrophied antral rugae. The duodenal cap was flattened on its superior surface. Prior to the onset of hematemesis, the patient's red count had been adequate, a typical example being that of March 4, 1946, when the red blood cells were 4,150,000 with 85 per cent hemoglobin. On April 15, the patient's red count was 3,600,000, but with the continuance of hematemesis it dropped to 1,930,000 by April 19, despite daily transfusions. The patient also received one to two pints of whole blood daily with a steady drop in the red count. During this period of hematemesis, no pain was complained of by the patient. It was decided, despite the wide spread metastatic process, to carry out an exploration on this patient since he was being ex-anguinated from the constant loss of blood from the stomach.

At operation, it was noted that the upper two feet of the jejunum were dilated with thickening of the wall and had a peculiar whitish aspect unlike the remainder of the small bowel. The stomach from its upper third downward was thickened, edematous, and seemed to be avascular. The duodenum was noted to be attached to the gall bladder by thick adhesions and these were loosened with a great deal of difficulty. The entire duodenum seemed to be involved in the fibrotic process previously noted in the jejunum. No large ulcer was noted in the stomach. Many oozing points, however, were noted in the edematous mucosa of the stomach. For the anastomosis, a portion of jejunum below the fibrotic area was chosen and thus left a very long proximal loop. This had to be done because of the apparent radiation injury to the upper portion of the jejunum. The entire surface of the resected stomach was noted to be hyperemic with multiple patches of hemorrhage and submucosal ecchymosis. The entire wall was thickened and edematous (Fig. 2).

Two days after operation it was noted that the patient's sclerae were yellow and by April 29 the skin was definitely icteric. No vomiting or nausea was noted for the first two weeks. Seven days postoperatively a fecal fistula developed at the site of the operative wound and it was felt that this probably arose from the long loop of jejunum which showed marked radiation effect at operation. The patient's condition deteriorated progressively with jaundice, fecal fistula, inability to eat, and occasional elevation of temperature. The patient was given supportive therapy by intravenous feedings and transfusions. Despite that therapy, emaciation continued progressively and the condition of the patient by June 1, 1946, was very poor. In the middle of June, 1946 it was noted that ingested food occasionally came out of the fistula in the abdominal wound which was about 15 cm. in diameter and 1 cm. deep. The patient continued to get weaker and died June 29, 1946.

Comment—This patient was admitted with rather widespread metastatic disease. The glands were present in the axilla and neck and there was a large retroperitoneal mass in the midabdomen which displaced the colon and both kidneys. The testicles were noted to be small and atrophic, but in the experience at this institution, this fact does not rule out primary testicular tumor in any metastatic disease, particularly when there is retroperitoneal metastasis. At any rate the patient received 5,880 r in forty four days with a 15 by 20 cm. portal. Moderately severe radiation illness was noted during treatment. There was noted shrinkage in the abdominal mass and six months after admission to this hospital a small increase in the size of the right testicle was noted which led to a right orchiectomy. Histologic diagnosis of testicular seminoma was then made. In addition to the metastases already mentioned, mediastinal metastatic involvement was noted six months after admission and treated with radiation with disappearance of the chest shadow. It will be noted that the patient received a large dosage of x-ray to the abdomen in a relatively short period of time. The onset of the gastrointestinal symptoms began about forty five days after

completion of therapy but was not very severe and did not require rigid ulcer regime. The gastrointestinal condition became serious approximately five months after the completion of radiation therapy when bloody vomitus was noted. There was no nausea or pain with the vomiting and clots of blood were noted in the vomitus. At no time was there massive hematemesis as was noted in the first case. It was postulated that the patient was probably having oozing from a bleeding ulcer. In this case where the metastatic process was so widespread there was some doubt as to the wisdom of abdominal operation but it was felt that the continuing loss of blood from the stomach would probably terminate in a fatality from that source unless something was done. Medical treatment was attempted and was of no avail. At operation, unfortunately, marked involvement of a good portion of the jejunum was noted despite which fact subtotal resection was done. The gross appearance on opening the stomach was that of ecchymosis and multiple patches of hemorrhage. The entire wall was thickened and edematous. In this case the patient did poorly because of the development of a fecal fistula at the site of the operative wound which probably arose from the long loop of jejunum that had shown such marked radiation effect at operation. The patient lived more than two months after the operation and in view of the widespread metastases as well as the widespread injury to the small bowel, complicated by the active bleeding from the stomach, it is felt that the operation was a temporary lifesaving procedure in a hopeless situation.

CASE 3—II, aged 30 years on March 1, 1946, noted swelling of the left testicle with no pain. The soldier was hospitalized and prostatic smears were reported to have shown acid fast bacilli. However, after a course of penicillin and sulfonamides he was returned to duty with a diagnosis of nonspecific epididymitis. Because of the continuance of the swelling, the patient was again hospitalized overseas and on the basis of laboratory findings evacuated to the United States with the diagnosis of tuberculous epididymitis on the left. Nine days after arrival in the United States a left orchiectomy was performed and a histologic diagnosis of embryonal carcinoma was made. The patient was transferred to Walter Reed General Hospital on Sept. 22, 1945 for further therapy.

On Oct. 2, 1945, a radical resection of the retroperitoneal nodes and spermatic vessels on the left side was done. Under anesthesia abdominal palpation revealed a large mass extending from the level of the umbilicus upward toward the left kidney. A large metastatic mass which had produced deviation of the left ureter on intravenous pyelography was noted to involve the ureteral wall and it was deemed necessary to perform a nephroureterectomy in addition to the removal of the large metastatic mass. Although the mass stripped off the aorta with ease, the fascia over the psoas muscle had become involved and in the mass the left renal vein was noted to be involved. Histologic examination of the removed metastatic mass revealed embryonal carcinoma. The patient withstood the operation without any complication.

From October 17 to December 11, the patient received forty-five x-ray treatments 5,200 r were given to each of the following portals: dorsolumbar, left suprapubic, umbilical, epigastric, lumbodorsal. This is a tumor dose of 5704 r at the level of the eleventh dorsal vertebra in fifty-five days. During the period of radiation, the patient had severe radiation sickness consisting of nausea and vomiting, but at the completion of treatment, began to improve. Weight increased from 131 to 140 pounds in the first three weeks after radiation therapy and no vomiting or abdominal pain was noted. The improvement continued until the middle of January, 1946, when he noticed epigastric pain followed in a few days by vomiting, particularly in the morning. Night pain was also persistent. The pain came on

usually two to three hours after eating and medication with belladonna and phenobarbital with frequent milk feeding seemed to afford some relief. Because of the extensive retroperitoneal metastasis, it was decided to give prophylactic irradiation to the mediastinum and left supraclavicular area. Accordingly, the patient received twenty x ray treatments from Feb 27 to March 26, 1946, with a total dose of 2,000 r to each of four portals over the thoracic cage. He also received five x ray treatments with a total dose of 2,000 r from Feb 27 to March 6, 1946, over the left supraclavicular area.

The patient stated that during this time there was also some overlapping of the radiation into the epigastric region. In the middle of March during the radiation he had violent radiation sickness and vomited several times a day. There was loss of appetite and a constant dull epigastric ache. The patient complained of passing a great deal of flatus both orally and by rectum. During this period, however, the vomitus was bile tinged and there was no blood or coffee grounds material noted. An upper gastrointestinal series done in January, 1946, revealed no pathology.

After the completion of the chest and supraclavicular radiation, the patient was granted a furlough and he felt fairly well for the first two weeks. Beginning in the first week of April 1946, a dull ache in the epigastrium was noted and again there was some vomiting. At this time the vomitus seemed markedly changed. It was usually dark brown in color and on one occasion bright red blood was noted. On April 20, the patient began to suffer with severe epigastric pain occurring two to three hours after eating and somewhat relieved by frequent milk feedings. During the next week, although the vomiting became less frequent, occurring every three to four days, the vomitus had a rich brown coloration. The stools were hard and dark brown. He was seen by a doctor in his home town who placed him on a soft diet with amphetol medication. However, the vomiting continued and there were sharp pains in the epigastrium which radiated to the right upper quadrant. In the first week of May, 1946, the patient noted marked weakness, anorexia, shortness of breath on the slightest exertion, palpitations of the heart, and fading images described as "blackout." Because of the weakness, the patient returned from furlough and physical examination revealed a markedly anemic, fatigued individual with marked pallor of all mucous membranes. Some tenderness on palpation of the epigastrium and in the upper right rectus region was obtained. Red blood cells were 2,100,000 with 5.89 Gm (33 per cent) of hemoglobin. The patient was given daily transfusions and placed on a rigid ulcer regime. An upper gastrointestinal x ray study on May 10 revealed marked narrowing of the antral portion of the stomach, and a spastic duodenum. No definite ulcer crater was demonstrated. Despite adequate medical treatment, the patient continued to vomit sporadically, the vomitus containing bright red blood.

Accordingly, the patient was prepared for surgery which was performed on May 14, 1946. At operation there was some fibrosis and edema in the abdominal musculature and there was more vascularity than is normally seen. The small intestine appeared normal except for slight thickening of a loop or two of the upper jejunum. The stomach in the region of the pylorus was greatly thickened, edematous, and had a whitish appearance. The liver appeared to be normal. A subtotal resection and a gastrojejunostomy were performed. On opening the stomach just proximal to the pyloric ring, an irregular ulcer 2 cm. in diameter and 2 mm deep, appearing to reach to the muscularis, was seen (Fig 3). In the pyloric portion of the stomach, the rugae appeared to be flattened and the mucosa appeared to be somewhat thickened and edematous with occasional small petechial hemorrhages. Microscopically, the mucosa exhibited moderate atrophic changes and evidence of edema. The most marked changes were seen in the submucosa, which was very edematous, with an increase of connective tissue elements and a mild increase in vascularity. The pathologists noted that the ulcer and stomach in general show a striking contrast to the usual gastric ulcer in that the mucosa in this case is atrophic, whereas in the ordinary gastric ulcer it is most often hyperplastic. The patient tolerated the operation fairly well and the post operative course was without incident. There was cessation of vomiting and epigastric pain. However, three weeks post-operatively the patient began to complain of abdominal

cramps with occasional diarrhea and poor appetite. He also complained of abdominal distention and the passage of a great deal of flatus by rectum. An upper gastrointestinal x-ray study was performed June 13, 1946, and a small ulcer niche in the anterolateral wall of the stoma was noted. There was some delay in the emptying time as a small residual of barium was noted at three hours in the stomach. However, at six hours, the stomach was empty. The mucosal pattern of the ileum was distorted, the walls being thickened and relatively fixed. The passage of barium through the small bowel was delayed and the meal had not reached the cecum in six hours. It was felt that there were changes in the small bowel, probably a result of radiation. Although the patient's appetite has improved and he has gained weight, physical examination shows marked distention of the abdomen, but no fluid is believed present. Occasional enemas relieve the distention for only a short period.

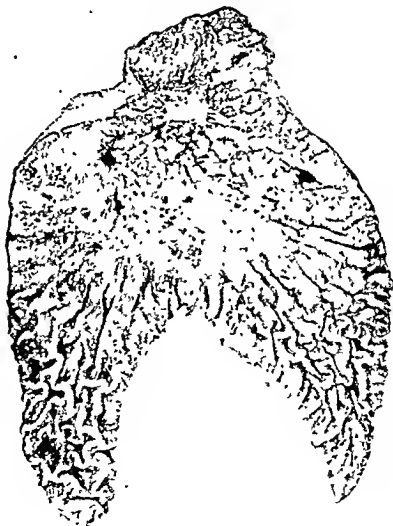


Fig. 3 (Case 3) — A large irregular ulcer is seen proximal to the pyloric ring. In the antrum there are areas of petichial hemorrhage and the wall is thickened.

Comment—This patient had an embryonal carcinoma of the testis with a large retroperitoneal metastatic mass. He received a tumor dose of 5304 r in fifty five days with a 10 by 10 cm portal. During radiation the patient had severe radiation sickness but there was improvement on completion. Gastrointestinal symptoms did not begin until thirty five days after completion of therapy. Additional radiation was given to the mediastinum prophylactically and there was some overlapping of the thoracic radiation onto the epigastrium. However, at the time the patient first complained of epigastric discomfort a gastrointestinal series did not reveal any pathology. It was not until four months later that the patient had severe epigastric distress with occasional bouts of vomiting. During this period the vomitus contained some blood. Four months after completion of the first course of radiation therapy hematemesis was noted with marked weakness and loss of blood. At operation some fibrosis, presumed due to radiation, was noted in the upper jejunum. The stomach revealed an ulcer in the pyloric region and petechial hemorrhages throughout the mucosa of the antrum. The postoperative course was uncomplicated for the first three weeks. At that time complaints of abdominal cramps with occasional diarrhea and anorexia were noted. X-ray studies revealed a small ulcer niche in the stoma. In summary we have been dealing with a case of widespread metastasis in which the prognosis from the start was very poor. Complications that have developed postoperatively were not a result of the operation which in this case, too, was a lifesaving procedure.

CASE 4—Y, aged 25 years, was in his usual state of good health until about April 1943 when he noticed pain in the umbilical region accompanied by nausea. About the same time swelling in the right scrotum together with hardness and enlargement of the right testicle was noted. Although there were no chills or fever the scrotum became warm and red. The pain in the scrotum became progressively worse and the patient was hospitalized overseas where he was treated with a suspensory and prostatic massage. Early in May 1943 a slightly tender swelling was noted in the right inguinal region. The pain continued for the next two months and the patient was evacuated to the United States on Aug. 21, 1943. He arrived at Walter Reed General Hospital Sept. 28, 1943.

Physical examination on admission to this institution revealed a large globular 4 fixed mass was also felt to the umbilicus. A testis and inguinal node was given and there was shrinkage in the size of the right testis of about 15 per cent and of the right inguinal nodes of about 85 per cent in one week. On Oct. 26, 1943, right orchiectomy with excision of the right external inguinal nodes was performed. The histologic examination of the testis revealed an embryonal carcinoma which showed marked radiation effect. Following the operation radiation therapy was continued and the patient received thirty six x-ray treatments from Oct. to Nov. 20, 1943 with a 12 by 20 cm portal over the anterior and posterior iliac regions for a dosage of 5500 r. This represented a tumor dose of 4,104 r in forty nine days at the level of the eleventh dorsal vertebra. At the completion of radiation therapy abdominal examination did not reveal the retroperitoneal mass previously palpated. The patient was granted a furlough and on return from the furlough complained of no symptoms. By the end of January 1944 the patient's general condition was good, weight was 165 pounds and no complaints referable to the upper gastrointestinal tract were present despite the tumor dose of 4,100 r to the center of the epigastrium. Prophylactic radiation was given to the mediastinum and left supraclavicular region the patient receiving

fourteen x ray treatments from Jan 10 to Jan 21, 1916, for a total dosage of 2,000 r to the suprapubic area, 1,500 r to both anterior and posterior mediastinal areas, and 1,200 r to the left supraclavicular area. Following this therapy the patient was granted another furlough.

While on furlough during February and March, 1916, the patient continued to gain weight and early in March weighed about 175 pounds, which was normal for him. About March 15, however, he began to notice pain in the epigastrium which he described as burning in type and being located over the entire epigastrium. This interval was four months after the last treatment to the abdomen and two and one half months after the last treatment to the mediastinum and suprapubic area. The patient did not notice any relationship to meals. The pain occurred sporadically and was usually accompanied by nausea and vomiting which afforded some relief. Night pain occurred frequently, accompanied by vomiting. There was no blood or coffee ground material noted in the vomitus. Tarry stools were not present. With the onset of the epigastric pain, his appetite became very poor and on return from furlough the patient had lost ten pounds. A gastrointestinal series done April 6, 1916, revealed marked narrowing of the stomach in the antral region. A filling defect was noted 3 cm proximal to the pyloric sphincter with a crater measuring 5 mm in diameter and 2 mm deep. Some hypertrophy of the valvulae conniventes was noted. The patient was placed on an ulcer regime and for the first month on the ward of the gastrointestinal section the patient seemed to improve. Sporadic attacks of exacerbating mid epigastric pain occurred. Gastroscopy on April 18, 1916, revealed reflux of bile from the duodenum with a patulous pylorus and a rigid antrum. Fractional gastric analysis on April 6, 1916, with Ewald meal revealed specimens of free hydrochloric acid of 11, 22, 49, 80 and 33 units. Repeat fractional gastric analysis with histamine on May 4, 1916, revealed specimens of free hydrochloric acid of 0, 0, 45, 72, and 46. Examination of the stools revealed occasional one to two plus occult blood. For the next month the patient's symptoms continued to get worse with intermittent attacks of epigastric pain and occasional vomiting. There was very little loss in weight, however, and no evidence of further metastasis of the primary disease. Repeat upper gastrointestinal study revealed an ulcer 3 by 2 cm in the distal portion of the antrum on the posterior wall. Because of the continuing pain which required moderate amounts of narcotics to control and in view of the x ray findings it was felt that the patient was probably having or had had a perforation of the antral ulcer. During this whole period of time there was no hematemesis noted and the patient had a comparatively normal blood picture. Hematocrit on May 21 was 37 volumes per cent and blood count on May 23 was 4,050,000 red cells with 81 per cent hemoglobin.

On May 26, 1916, laparotomy was performed. The liver appeared to be somewhat smaller than normal. The stomach was seen to be elephantine and vascular, and just above the pylorus an indurated area with a crater was felt on the posterior wall. The upper two feet of the jejunum were noted to be whitish, thickened, and edematous. It was felt that the duodenum was free enough of radiation injury to justify resection. On following the stomach posteriorly, a perforation of the posterior wall of the stomach into the pancreas and transverse mesocolon was encountered (Fig 4). A subtotal gastrectomy and gastrojejunostomy were performed. The jejunum selected for the anastomosis was below the fibrotic area previously described. The patient's immediate postoperative course was uneventful and one month after operation the patient was transferred back to the gastrointestinal section for further care. At the end of June 1916 the patient was asymptomatic and ambulatory with complete relief of the preoperative symptoms.

However, in the second week of July, 1916, the patient started to complain of periodic generalized abdominal pains particularly below the umbilicus. There was a slow weight gain and his appetite remained good, but the pains in the lower abdomen have continued to the time of this writing. There has been no evidence of bleeding. The patient also complains of distention and flatus and is having two bowel movements, not particularly

of the upper gastrointestinal tract revealed a normally functioning stomach with no evidence of stomal ulcer. Mucosal pattern of the colon, however, barium enema performed July 24, 1946, revealed a shortening in length in the mid portion of the transverse colon which is associated with mucosa that appears to be ulcerated. At the time of operation, no symptoms continue.

At one year postoperatively the patient was fairly well with occasional lower abdominal pain relative to a colitis secondary to radiation.



FIG. 4 (Case 4).—Perforation of the posterior wall of the stomach.

Comment—This patient had an embryonal carcinoma of the testicle with right inguinal and retroperitoneal nodal metastasis. He was given a tumor dose of 6105 r in forty nine days with a 15 by 20 cm. portal at the completion of which time abdominal examination did not reveal the retroperitoneal mass previously palpated. Additional radiation was given to the mediastinum and left supraclavicular area. Gastrointestinal symptoms began about four months after the completion of radiation to the epigastrium. In this case medical treatment was not successful in relieving the pain and the marked loss of appetite that the patient had. In view of the excruciating attacks of pain and the vomiting which occurred during these episodes it was felt that the possibility of perforation having taken place was a good one. In this case no bleeding occurred prior to operation but it was felt that operation was indicated because of the terrific pain and discomfort that the patient had. Impression of perforation was confirmed at operation and it was noted that the upper two feet of the jejunum were probably also affected by the radiation. It is well to note that the portal used in this case was rather large and covered a larger area than some of the other cases. The postoperative course was good and for the first month the patient was asymptomatic with complete relief of preoperative symptoms. One and one half months after operation however the onset of lower abdominal pain was noted with distention and flatus and slight diarrhea. A barium enema revealed the mid portion of the transverse colon to be ulcerated probably the result too of radiation. The indication for this operation was the perforation and the lack of relief of symptoms obtained by medication.

patient's weight was maintained at 145 pounds and another upper gastrointestinal tract series was obtained. On this examination of March 13, hypertrophy of the mucous membrane of the antral portion of the stomach was noted and there was a suggestion of a possible area of ulceration of the greater curvature in the antral portion. However no crater could be demonstrated. In view of the symptomatology and the x-ray findings the patient was transferred to the gastrointestinal station April 20, 1946.

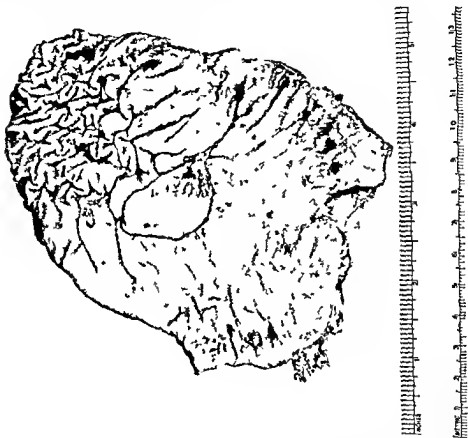


Fig. 2 (Case 5) —Ulcer found in the pyloric rim, mucous membrane is thickened and edematous.

The patient complained of pain in the epigastrium which came on three to four hours after eating. The pain was relieved by eating and milk seemed to afford a good deal of comfort. Occasional attacks of nausea and night pain were also noted. Fractional gastric analysis with histamine on March 13, 1946 revealed specimens containing 0.077 cc and 2 units of free hydrochloric acid. Caesarean operation performed April 20, 1946 revealed a rigid antrum but no ulcerations were noted. Repeat gastrointestinal series on April 20 showed in addition to the narrowing in the antrum a contracted and irregular duodenal cap. The patient was placed on a rigid ulcer regime and for the first several weeks there seemed to be some improvement in the patient's symptoms. However there were sporadic attacks of severe epigastric pain which increased in frequency by the middle of May 1946. At this time the attacks of pain were accompanied by vomiting and on several occasions small amounts of bloody material were noted in the vomitus. The patient had days during which he experienced little pain and vomiting and other days during which there were many attacks

Comment—This patient had an embryonal carcinoma of the testicle with right inguinal and retroperitoneal nodal metastasis. He was given a tumor dose of 6,105 r in forty nine days with a 15 by 20 cm portal, at the completion of which time abdominal examination did not reveal the retroperitoneal mass previously palpated. Additional radiation was given to the mediastinum and left supraclavicular area. Gastrointestinal symptoms began about four months after the completion of radiation to the epigastrium. In this case medical treatment was not successful in relieving the pain and the marked loss of appetite that the patient had. In view of the excruciating attacks of pain and the vomiting which occurred during these episodes it was felt that the possibility of perforation having taken place was a good one. In this case, no bleeding occurred prior to operation but it was felt that operation was indicated because of the terrific pain and discomfort that the patient had. Impression of perforation was confirmed at operation and it was noted that the upper two feet of the jejunum were probably also affected by the radiation. It is well to note that the portal used in this case was rather large and covered a larger area than some of the other cases. The postoperative course was good and for the first month the patient was asymptomatic with complete relief of preoperative symptoms. One and one half months after operation however, the onset of lower abdominal pain was noted with distention and flatulence and slight diarrhea. A barium enema revealed the mid portion of the transverse colon to be ulcerated probably the result too of radiation. The indication for this operation was the perforation and the lack of relief of symptoms obtained by medication.

CASE 3—B, age 12½ year, was in his usual state of health until June 1943 when while playing baseball he injured his left hip. Two days later swelling of the left scrotum was noted. The patient was seen on such call and treated but was returned to duty in four days. However the swelling continued and he was finally hospitalized in September 1943 at which time a left orchidectomy was performed. Histologic diagnosis of carcinoma was made postoperatively. The patient was evacuated to the United States and admitted to this hospital Oct. 21 1943.

It was decided to treat this patient with radiation and this was begun on Oct. 26 1943. From that date until Dec. 23 1943 the patient received forty five x-ray treatments 5000 r being given to the following portals: Left suprapubic umbilical epigastric lumbo-sacral lower dorsal. This delivered a tumor dose of 5000 r at the level of the eleventh dorsal vertebra in fifty four days. Radiation sickness during the period of treatment was moderately severe with generalized abdominal pains nausea and occasional vomiting. Although his appetite was poor weight remained stationary. Because of the severe radiation sickness and the awareness at that time of the possibility of gastric injury an upper gastrointestinal radiograph was obtained and was reported to be negative. Treatment was therefore continued until the final radiation in good general condition. The patient was granted a furlough at the completion of therapy and on return stated that he had felt fairly well in the past month. However he complained of epigastric distress which was relieved somewhat by food. At that time there was no vomiting but there had been occasional attacks of nausea with pain which was localized to the midepigastrium without radiation. The patient denied ever having had any symptoms referable to the gastrointestinal tract prior to the onset of radiation therapy. Because of the continuing abdominal complaints a gastrointestinal series was obtained on January 20 and was reported to be negative. For the next two months the patient continued to complain of epigastric discomfort. The

tion injury that did not respond fairly promptly to medical treatment would probably not respond at any time to medical treatment and surgery was indicated prior to the onset of complications. At operation only slight changes were noted in the jejunum and transverse colon. An ulcer in the pyloric region was revealed on opening the stomach. That the postoperative course would not be uncomplicated is indicated by the small intestinal changes that have already made their appearance by radiologic examination.

CASE 6—Ty, a 22 year old white soldier, was in his usual state of health until February, 1945, when he noted that the left testis was harder and larger than usual. There was no pain or history of injury. In August, 1945, the left testicle which had now grown larger was diagnosed as a tumor and the patient was evacuated to the United States. He was admitted to Walter Reed General Hospital, Sept. 29, 1945.

Physical examination was negative except for a hard, heavy, irregular, nontender left testicle slightly larger than normal. On Oct. 9, 1945, a radical left orchiectomy was performed and no metastases were found in the retroperitoneal nodes. Histologic diagnosis of the testicular tumor was teratoma mixed type (teratocarcinoma). This operation was complicated by an incisional abscess which was treated by incision, drainage, and penicillin. When this had healed, the patient was started on prophylactic irradiation and he received 4,500 r at the level of the eleventh dorsal vertebra from Nov. 12, 1945, to Jan. 4, 1946, in fifty three days.

During radiation the patient had very little difficulty. About six days after the completion of treatment, he had many gastrointestinal complaints: pain, belching, nausea, and occasional vomiting. These complaints were continuous and persistent. The patient would describe the pain as being severe and cramplike, coming on during the night when the stomach was empty. Occasional relief was obtained by food. Ice cream was well tolerated and relieved the pain whereas milk or cream caused nausea. Because of these complaints on Jan. 24, 1946, twenty four days after completion of therapy, an upper gastrointestinal series was obtained and showed no evidence of an organic lesion of the esophagus, stomach, duodenum, or small intestine. However, the patient continued to complain of epigastric pain and sporadic attacks of vomiting. Because of the persistent continuing complaints, he was transferred to the gastrointestinal section. A repeat x-ray series on February 28 revealed marked changes in the stomach since the previous radiographic examination. The antral mucosal folds were distorted and thickened. A deformity simulating an ulcer crater was noted in the antrum and the duodenal cap showed evidence of disease without ulceration. The patient was placed on a strict ulcer regime with supplemental analgesic medication and began to do fairly well with the exception of occasional epigastric pain. On March 2, 1946, fractional gastric analysis with histamine revealed no free hydrochloric acid in all specimens. The blood counts and hematocrit remained normal until the latter part of March, when a slight drop in the red count was noted. A repeat gastric analysis on March 16 showed specimens containing 0, 0, 35, 25 and 20 units of free hydrochloric acid. The episodes of occasional sporadic epigastric pain continued and about April 1, specimens of the feces showed occult blood at rather frequent examinations. A repeat upper gastrointestinal series on May 3, 1946, showed continuation of the process noted in the stomach. In the latter part of the anemia which required transfusion.

ward and it was noted that he was very pale, the blood count was 2,300,000 with a hematocrit of 23. The patient had been having three to four loose bowel movements for three days prior to the episode of syncope and it was felt that the bleeding was coming from the ulcer noted by x-ray in the stomach. The episodes of pain remained to a lesser degree during this period.

Gastroscopic examination April 13 showed a rigid, stiff antrum but no ulceration could be noted. The pylorus was noted to be patent and there was reflux bile noted which obstructed the view of the mucosa in the antrum.

of pain and vomiting. It was felt that the patient was showing little improvement on a medical regime and a radiographic study on May 24, 1946, showed progressing changes in the antrum and in the duodenum. It was thought that ulceration was present in the pyloric region although a definite niche was not demonstrated. Stool examinations were noted to contain occult blood on several occasions. By the middle of June, 1946, the patient was having excruciating pain and attacks of vomiting during which small quantities of fresh blood were noted in the vomitus.

Because of the apparently progressing nature of the disease, it was felt that subtotal gastrectomy was indicated before further complications, such as massive hemorrhage or perforation, made themselves evident. Accordingly, the operation was performed on June 2, 1946. At operation there was evidence of increased fibrosis and alteration in the color of the stomach. Slight changes believed to be due to radiation fibrosis were also noted in the jejunum and transverse colon. In the right flank a serosanguineous exudate which had the appearance of thin watery pus was found. However, no abscesses could be found and examination of the stomach did not reveal grossly a perforation. The antrum of the resected portion of the stomach showed petechial hemorrhages throughout. The mucous membrane was noted to be greatly thickened and extremely edematous. In the pyloric ring just posterior to the lesser curvature an ulcer 1.8 by 1.7 cm was noted. This ulcer was approximately 0.6 cm. deep (Fig 5). It was felt that the edema surrounding the pyloric ring must have practically occluded the lumen of the pylorus. Histologic picture was similar to that found in other stomachs altered by radiation.

Following the operation the patient did well until the mid part of July when he began to have episodes of nausea and vomiting. The vomiting came on at irregular periods and on one occasion 1,300 c.c. of retained gastric contents were aspirated. Because of the continuance of vomiting barium study was performed and it showed no evidence of a stomal ulcer. A normally functioning gastroenterostomy was noted as well as moderate hypertrophy of the mucosal markings and thickening of the walls of the distal ileum. The patient was transferred back to the gastrointestinal section and has had continuing episodes of nausea and vomiting which come on at irregular periods and in no definite pattern. Despite these attacks of nausea and vomiting, the patient has been completely relieved of the excruciating pains that he had with the attacks prior to operation. It is discouraging to note, however, that small intestinal changes have already appeared by x ray.

Comment—This patient had a carcinoma of the testis and after orchidectomy overseas was transferred to this installation. He received a tumor dose of 5,096 r at the level of the eleventh dorsal vertebra in fifty four days with a 10 by 10 cm portal. During radiation he experienced moderately severe radiation illness. During the period of these symptoms an upper gastrointestinal study was negative. About thirty days after completion of treatment another gastrointestinal series was obtained and again a negative report was received. However, the patient continued to complain of epigastric discomfort which was rather mild, but became increasingly severe. X ray changes were first noted three and one half months after completion of therapy. This patient had sporadic attacks of epigastric pain with nausea and vomiting that continued despite rigid medical treatment for two months. During this period there were also progressive changes by x ray and the patient's appetite was becoming poorer with concomitant loss of weight. Although it was not felt that any complications were present, operation seemed indicated because of the progressive nature of the patient's condition and because by this time it was felt that such cases of radia-

*Surgery performed by Lieutenant Colonel Frank F. Hamilton, Walter Reed General Hospital.

However, some patients with ulcers demonstrable by x ray and/or gastroscopy have shown a tendency to improve under medical care. It remains a matter of individual case judgment as to when surgery is required.

The operative therapy requires moderately radical partial gastrectomy. In this group of cases a Hofmeister type of procedure was utilized. Any method could be employed except the Billroth I type which requires end-to-end anastomosis of the incised end of the stomach to the duodenal stump. Because the duodenum is occasionally involved in the radiation effect it is believed that healing may be delayed or faulty healing may induce a fatal outcome if the end-to-end anastomosis is employed. The operation therefore is similar to that used for the radical treatment of ordinary peptic ulcer.

The differences and difficulties reside in the altered pathologic picture. It has been mentioned that the skin and abdominal wall are relatively free of the radiation changes. When the abdomen is opened preferably by a transverse incision which allows better exposure one can see the lesion which is characterized by an edematous thickened whitish appearance and when palpated is definitely firmer than the normal stomach. The jejunum and duodenum are apt to show more of the white discoloration than the stomach. In Cases 1 and 4 a large penetrating ulcer with indurated edges could be felt. Both ulcers were in the pyloric region and posteriorly. The vascularity was increased in all cases particularly in the region of the first portion of the duodenum. Cases 2 and 3 demonstrated a generalized radiation effect without formation of large ulcers. It is conceivable that many small ulcers were present before medical treatment brought about healing.

The greatest difficulty in the operation is to establish whether or not the radiation effect can be completely eradicated at the duodenal end. The pathologic process gradually melts away into normal stomach or duodenum. The duodenal line of incision is limited because of the presence of the pancreatic and common bile ducts. The gastric line of incision could be more certainly established because the fundus of the stomach is out of the line of the x ray portals and one is able to incise the stomach at a point known to be above the radiation change. In Case 2 the duodenum although less involved than the stomach was involved to such an extent that faulty healing was anticipated. One is not so much concerned with the presence of the process in the first part of the jejunum because an anastomosis below the lesion in the jejunum can be accomplished. In Case 2 because of widespread jejunal injury better judgment would have been to abandon the procedure and that would have been done except for the fact that the patient was obviously dying of uncontrollable hemorrhage. The risk of healing of the duodenal stump and anastomosis was felt to be his only chance for survival.

It was feared that the necessary manipulation for mobilization of the duodenum and the freeing of the curvatures might induce a hemorrhage which would be fatal in the chronic anemic state of the patients. In Case 1 the operator fortunately saw the gush of blood from the large branch of the middle colic vein which could be easily controlled by clamping under direct vision. None

On June 12, a left supraclavicular nodal enlargement was noted which was shown by biopsy to be metastatic teratoma. To this area the patient received 2,700 r in nine treatments from June 14, 1946, to June 29, 1946, with shrinkage of the left supraclavicular nodes. There was continuous bleeding through the lower bowel, necessitating repeated transfusions to relieve the anemia. The pain continued intermittently but was not as severe as it was in the early stages of the gastric disease. Repeat x ray on June 19, 1946, revealed a 2 cm. ulcer on the greater curvature side of the antrum. A patulous pylorus was noted and the distal half of the body of the stomach and antrum were narrow and fixed with atrophic rogae.

In the latter part of July, the patient noted a tender area in the left upper epigastrium which over a two week period became very tender and painful to palpation. Physical examination revealed a small tender mass in this area. In view of the fact that this patient was bleeding to the extent that he needed one to two transfusions of whole blood weekly for some time, and in view of the fact that an ulcer was demonstrated by x ray, it was felt that this mass could well represent a walled off abscess, secondary to perforation of the ulcer. In view of the constant and continuing blood loss in the past several months without any alleviation by a medical regime, and because of the recent development of the left epigastric mass, it was felt that surgery was indicated without delay.* On Aug. 15, 1946, the patient was operated upon and on opening the free peritoneal cavity, there was found purulent material in the lesser omental sac and the stomach was noted to be bound down in a mass of adhesions which existed between the transverse colon and the duodenum. There was a small walled-off abscess between the posterior wall of the stomach and the transverse colon which was separated with difficulty. Marked adhesions were noted on the serosal surface of the stomach in the greater curvature area. It was also noted at operation that a good portion of the jejunum was involved in the radiation fibrosis and it was with some difficulty that a portion sufficient for anastomosis was found. A partial resection of the stomach was done and a portion of the first part of the duodenum was removed. On opening the resected specimen, there was a 3 by 2 by 3 cm. triangular ulceration on the greater curvature posterior wall of the stomach. The ulcer was about 6 mm deep and had a hard fibrotic base. In the middle of it there was a smaller deeper area 1 by 0.5 cm through which apparently the perforation had occurred, although there was no obvious perforation noted since the serosal surface had been completely walled off by adhesions.

Comment—This patient had metastatic disease for which 4,800 r were given at the level of the eleventh dorsal vertebra in fifty three days. Symptoms were noted quite some time before x ray changes developed. Despite the presence of anemia and blood in the feces, a medical regime was carried on for a long while. The development of an epigastric mass indicated that a new complication of the ulcer had appeared. Operation performed 223 days after completion of radiation revealed peritonitis secondary to a subacute perforation of a large antral ulcer. The patient's postoperative course has thus far been uncomplicated.

SURGICAL OBSERVATIONS

The indications for surgery in this group of cases differ little from the indications for surgery in peptic ulcer. Perforation, hemorrhage, and intractability of symptoms have been the indications in the series presented. Possibly, surgical intervention at an earlier period is indicated in those cases of ulcer secondary to radiation that do not respond rather quickly to a medical regime. In proportion to the number of cases observed, the complications occur in greater proportion than in ordinary peptic ulcer. The well known fact that radiation injury tends to be progressive also lends support to earlier surgical intervention.

*Surgery performed by Lieutenant Colonel Frank E. Hamilton, Walter Reed General Hospital.

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The operative therapy requires moderately radical partial gastrectomy. In this group of cases a Hofmeister type of procedure was utilized. Any method could be employed except the Billroth I type which requires end to end anastomosis of the incised end of the stomach to the duodenal stump. Because the duodenum is occasionally involved in the radiation effect it is believed that healing may be delayed or faulty healing may induce a fatal outcome if the end to end anastomosis is employed. The operation therefore is similar to that used for the radical treatment of ordinary peptic ulcer.

The differences and difficulties reside in the altered pathologic picture. It has been mentioned that the skin and abdominal wall are relatively free of the radiation changes. When the abdomen is opened preferably by a transverse incision which allows better exposure one can see the lesion which is characterized by an edematous thickened whitish appearance and when palpated is definitely firmer than the normal stomach. The jejunum and duodenum are apt to show more of the white discoloration than the stomach. In Cases 1 and 4 a large penetrating ulcer with indurated edges could be felt. Both ulcers were in the prepyloric region and posteriorly. The vascularity was increased in all cases particularly in the region of the first portion of the duodenum. Cases 2 and 3 demonstrated a generalized radiation effect without formation of large ulcers. It is conceivable that many small ulcers were present before medical treatment brought about healing.

The greatest difficulty in the operation is to establish whether or not the radiation effect can be completely eradicated at the duodenal end. The pathologic process gradually melts away into normal stomach or duodenum. The duodenal line of incision is limited because of the presence of the pancreatic and common bile ducts. The gastric line of incision could be more certainly established because the fundus of the stomach is out of the line of the x ray portals and one is able to incise the stomach at a point known to be above the radiation change. In Case 2 the duodenum although less involved than the stomach was involved to such an extent that faulty healing was anticipated. One is not so much concerned with the presence of the process in the first part of the jejunum because an anastomosis below the lesion in the jejunum can be accomplished. In Case 2 because of widespread jejunal injury better judgment would have been to abandon the procedure and that would have been done except for the fact that the patient was obviously dying of uncontrollable hemorrhage. The risk of healing of the duodenal stump and anastomosis was felt to be his only chance for survival.

It was feared that the necessary manipulation for mobilization of the duodenum and the freeing of the curvatures might induce a hemorrhage which would be fatal in the chronic anemic state of the patients. In Case 1 the operator fortunately saw the gush of blood from the large branch of the middle colic vein which could be easily controlled by clamping under direct vision. None

A STUDY OF THE GASTRIC STOMA AFTER PARTIAL GASTRECTOMY

AN ANALYSIS OF NINETY GASTRIC RESECTIONS

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(From the Grace Hospital)

IN FORMER years we used to hear a great deal about the "stoma" that was made between the stomach and jejunum when a gastroenterostomy was done. Surgeons always made a point of demonstrating to their assistants and the admiring audience that the stoma at the site of the anastomosis was of good size and well placed. It was felt then that if this was done the operation would be a success. Surgeons went on making bigger and better stomas in the erroneous belief that patients with peptic ulcers would be cured. With the passage of time however it was soon found among thinking surgeons that regardless of the size or position of the stoma these patients were not being cured. It was quite evident that the size or position of the stoma had nothing whatever to do with the success of the operation. It has been demonstrated rather conclusively that to be successful an operation for peptic ulcer must remove the maximum possible amount of gastric mucosa containing acid forming glands and the antral mucosa.²

It is generally felt among surgeons that the stoma is the entire diameter of the stomach that is used in the anastomosis.³ Thus in the Polya operation the stoma would be very large and in the Hoffmeister operation it would be much smaller.

In our series of ninety cases the Polya type of anastomosis was the surgical procedure used except for seven cases in which a Hoffmeister modification was employed. This was found very useful in those cases in which the lesion was unusually high up on the lesser curvature and a safer anastomosis could be made by closing a part of the stomach stoma.

Eighty one of the patients operated upon were men and only nine were women. Sixty eight of the patients were operated upon for duodenal ulcers and twenty one had gastric ulcers. One patient had a marginal ulceration. Our youngest patient was 22 years old and the oldest was 72 years old.

After studying roentgenograms and sketches made from them of these resections we were led to the conclusion that the "true stoma" that resulted from partial gastrectomy was not the currently held wide diameter of the residual stomach but was rather the narrow jejunal diameter into which the stomach empties (see Fig 1). From an examination of Fig 1 it is quite evident that the stomach can empty only as fast as the luminal diameter of the jejunum

TABLE I PATIENTS OPERATED UPON

NAME	SEX	AGE	DISEASE	OPERATION	RESULTS
1 H C	M	27	Duodenal ulcer	Subtotal gastrectomy	Good
2 L B M	F	27	Gastric ulcer	Subtotal gastrectomy	Good
3 J K	M	27	Duodenal ulcer	Subtotal gastrectomy	Good
4 J K	M	27	Gastric ulcer	Subtotal gastrectomy	Good
5 S I G	M	30	Duodenal ulcer	Subtotal gastrectomy	Good
6 G N	M	32	Duodenal ulcer	Subtotal gastrectomy	Good
7 G H	M	32	Duodenal ulcer	Subtotal gastrectomy	Good
8 W W R	M	32	Duodenal ulcer	Subtotal gastrectomy	Good
9 H L	M	31	Duodenal ulcer	Subtotal gastrectomy	Good
10 J C	M	34	Gastric ulcer	Subtotal gastrectomy	Good
11 C H	M	36	Duodenal ulcer	Subtotal gastrectomy	Good
12 A L T	F	39	Duodenal ulcer	Subtotal gastrectomy	Good
13 W F G	M	40	Duodenal ulcer	Subtotal gastrectomy	Good
14 C M	M	41	Duodenal ulcer	Subtotal gastrectomy	Good
15 T S	F	41	Gastric ulcer	Subtotal gastrectomy	Good
16 L E	M	41	Duodenal ulcer	Subtotal gastrectomy	Good
17 H A	M	41	Duodenal ulcer	Subtotal gastrectomy	Good
18 J H	M	42	Gastric ulcer	Subtotal gastrectomy	Good
19 R T	M	42	Duodenal ulcer	Subtotal gastrectomy	Good
20 M R	M	42	Duodenal ulcer	Subtotal gastrectomy	Good
21 C M	M	42	Duodenal ulcer	Subtotal gastrectomy	Good
22 H G	M	44	Gastric ulcer	Subtotal gastrectomy	Good
23 T J	M	44	Duodenal ulcer	Subtotal gastrectomy	Good
24 L V	M	45	Duodenal ulcer	Subtotal gastrectomy	Good
25 G A	M	45	Duodenal ulcer	Subtotal gastrectomy	Good
26 R S L	M	44	Duodenal ulcer	Subtotal gastrectomy	Good
27 W M	M	44	Duodenal ulcer	Subtotal gastrectomy	Good
28 S J M	M	44	Duodenal ulcer	Subtotal gastrectomy	Good
29 A W	M	47	Gastric ulcer	Subtotal gastrectomy	Good
30 D H	M	47	Duodenal ulcer	Subtotal gastrectomy	Good
31 J H M	M	47	Duodenal ulcer	Subtotal gastrectomy	Good
32 H L	M	47	Duodenal ulcer	Subtotal gastrectomy	Good
33 A B	M	48	Duodenal ulcer	Subtotal gastrectomy	Good
34 J B E	M	48	Duodenal ulcer	Subtotal gastrectomy	Good
35 O F H	M	49	Duodenal ulcer	Subtotal gastrectomy	Good
36 A P	M	47	Duodenal ulcer	Subtotal gastrectomy	Good
37 C T W	M	48	Gastric ulcer	Subtotal gastrectomy	Good
38 F R	M	48	Duodenal ulcer	Subtotal gastrectomy	Good
39 C R	M	50	Duodenal ulcer	Subtotal gastrectomy	Good
40 M F F	F	50	Gastric ulcer	Subtotal gastrectomy	Good
41 W G	M	50	Duodenal ulcer	Subtotal gastrectomy	Good
42 A M	F	50	Marginal ulcer	Subtotal gastrectomy	Good
43 K H	M	51	Duodenal ulcer	Subtotal gastrectomy	Good
44 E D S	M	51	Duodenal ulcer	Subtotal gastrectomy	Good
45 E M	M	51	Duodenal ulcer	Subtotal gastrectomy	Good
46 L B	M	51	Duodenal ulcer	Subtotal gastrectomy	Good
47 J M	M	51	Gastric ulcer	Subtotal gastrectomy	Good
48 A M	M	52	Duodenal ulcer	Subtotal gastrectomy	Good
49 F K	M	52	Duodenal ulcer	Subtotal gastrectomy	Good
50 W B	M	52	Duodenal ulcer	Subtotal gastrectomy	Good
51 I W	M	52	Duodenal ulcer	Subtotal gastrectomy	Good
52 J J	M	52	Duodenal ulcer	Subtotal gastrectomy	Good
53 K K	M	54	Duodenal ulcer	Subtotal gastrectomy	Good
54 C W G	M	54	Duodenal ulcer	Subtotal gastrectomy	Good
55 K H	M	54	Duodenal ulcer	Subtotal gastrectomy	Good
56 H M	M	55	Gastric ulcer	Subtotal gastrectomy	Good
57 F G	F	55	Duodenal ulcer	Subtotal gastrectomy	Good
58 W P M	M	55	Duodenal ulcer	Subtotal gastrectomy	Good
59 G M	M	55	Duodenal ulcer	Subtotal gastrectomy	Good
60 H B	M	56	Duodenal ulcer	Subtotal gastrectomy	Good
61 E E	M	56	Gastric ulcer	Subtotal gastrectomy	Good
62 M S	M	56	Gastric ulcer	Subtotal gastrectomy	Good
63 J H	F	58	Gastric ulcer	Subtotal gastrectomy	Good
64 R H	M	58	Gastric ulcer	Subtotal gastrectomy	Good

TABLE I (CONT'D)

NAME	SEX	AGE	DIAGNOSIS	OPERATION	RESULTS
65 A W	M	59	Duodenal ulcer	Subtotal gastrectomy	Good
66 T P	M	54	Gastric ulcer	Subtotal gastrectomy	Good
67 J H C	M	74	Duodenal ulcer	Subtotal gastrectomy	Good
68 A B	M	57	Duodenal ulcer	Subtotal gastrectomy	Good
69 C E	M	57	Gastric ulcer	Subtotal gastrectomy	Good
70 J L	M	57	Duodenal ulcer	Subtotal gastrectomy	Good
71 M C	M	54	Duodenal ulcer	Subtotal gastrectomy	Good
72 J W	M	51	Duodenal ulcer	Subtotal gastrectomy	Good
73 L P	F	36	Duodenal ulcer	Subtotal gastrectomy	Good
74 H W	M	51	Duodenal ulcer	Subtotal gastrectomy	Good
75 W H	M	60	Duodenal ulcer	Subtotal gastrectomy	Good
76 M D	M	60	Duodenal ulcer	Subtotal gastrectomy	Good
77 T H H	M	61	Gastric ulcer	Subtotal gastrectomy	Good
78 J D	M	61	Duodenal ulcer	Subtotal gastrectomy	Good
79 G A H	M	62	Gastric ulcer	Subtotal gastrectomy	Good
80 H F	M	62	Duodenal ulcer	Subtotal gastrectomy	Good
81 J C C	M	62	Gastric ulcer	Subtotal gastrectomy	Good
82 J K	M	64	Duodenal ulcer	Subtotal gastrectomy	Good
83 G M	M	66	Duodenal ulcer	Subtotal gastrectomy	Good
84 J G	F	66	Duodenal ulcer	Subtotal gastrectomy	Good
85 D W O	M	71	Duodenal ulcer	Subtotal gastrectomy	Good
86 E G B	M	77	Gastric ulcer	Subtotal gastrectomy	Good
87 G P	M	72	Duodenal ulcer	Subtotal gastrectomy	Good
88 H W	M	47	Duodenal ulcer	Subtotal gastrectomy	Good
89 A K	M	36	Duodenal ulcer	Subtotal gastrectomy	Good
90 B C	M	57	Duodenal ulcer	Subtotal gastrectomy	Good

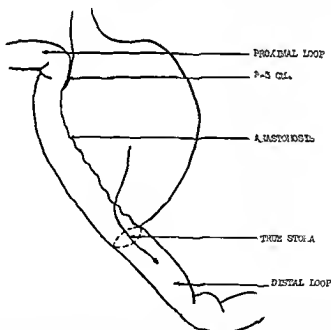


Fig. 1—Note that a Polya type of resection has been done. The proximal loop has been sutured along the lesser curvature for two to three centimeters. Note the true gastric stoma as being the lower end of the anastomosis and consisting of the circumference of the jejunum into which the stomach empties.

to which it is attached can accommodate its contents. Since the proximal loop of jejunum is nonfunctional (see Figs 2 and 3) that portion of the jejunum along the entire length of the anastomosis becomes actually merely a part of the stomach wall (see Fig 2). If we disregard the proximal loop which we must since it is nonfunctional it would be quite evident that only the lower end of the anastomosis becomes part of the true gastric stoma. As an analogy if one considers the remaining stomach with the jejunum as being its lower wall as a funnel which in truth it is then the stoma must of necessity be that narrowed portion which carries the gastric contents into the jejunum. A glance at Fig 1 readily shows that this must be only at one point and not along the entire length of the anastomosis. This point becomes more obvious if one will note that in Fig 5 which was taken four years following gastrectomy the lower gastric wall (jejunum) has bulged considerably downward almost restoring the original size of the stomach but the true gastric stoma which is now displaced to the left still remains the same caliber. Fig 3 represents the stomach and jejunum including the anastomosis removed from a patient at autopsy.



A

B

— R. T. S. A.

This patient had been operated upon four days previously (not by us) and had suddenly died of coronary occlusion. We removed the stomach in toto and injected barium through the esophagus. The stomach was then held up by the esophagus and the barium permitted to run downward. Roentgenograms were then taken (Fig 3). Note that here too there is no barium in the proximal loop and that the main stream of barium runs downward through the true

gastric stoma. It is quite evident that the stream of barium, when seen under fluoroscopy, runs along the lesser curvature striking the jejunal wall and then rebounding to the greater curvature and passing through the true gastric stoma. Since this is then the true gastric stoma, great care must be taken in performing the anastomosis to prevent rotation of the jejunum onto the greater curvature of the stomach which so commonly produces obstruction at the lower end of the anastomosis and so obstructs the true gastric stoma with disastrous consequences.

A study of roentgenograms (Figs 2 and 4), taken several years postoperatively shows rather well that the barium passes through this stoma as it would through the pylorus.



Fig 3

Fig 3—Autopsy specimen. Note that there is no barium in the proximal loop. Note that the barium stream passes through the lower end of the anastomosis that is true gastric stoma.



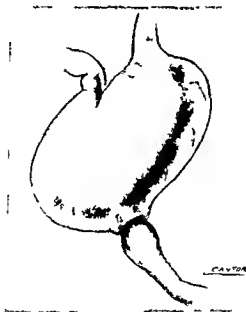
Fig 4

Fig 4—Note the out pouching of the jejunal wall producing a relative displacement of the true gastric stoma to the left. Note the constriction of the barium stream at the true gastric stoma suggesting sphincteric action at this point.

During the first week postoperatively due to stomal edema there are always varying amounts of gastric retention dependent upon the degree of edema at the true gastric stoma. The retained fluids are siphoned off by the use of a Levin tube. If the entire circumference of the anastomosis were the true outlet, it would take a tremendous amount of edema to produce a delay in gastric emptying much less a retention. Because the true gastric stoma is that small funnel like opening at the lower end of the anastomosis, a slight amount of edema at this point readily impedes gastric emptying. Even after all

edema has subsided such patients must be warned not to eat too much or too fast because the narrowed gastric outlet is not large enough to permit the passage of solid foods through it very rapidly. On the other hand liquid foods might pass through the stoma faster than the loop of jejunum into which it empties can accommodate it. Again the patient would suffer from epigastric distress.

With the passage of time and the gradual enlargement of the residual stomach and its jejunal wall by stretching it becomes possible for such patients to eat larger meals without discomfort. If it were true that the entire width of the remaining portion of the stomach were the stoma this could not occur because emptying would occur too rapidly for the stomach ever to become distended and so stretched. Clinical observations of patients subjected to



Note the out-
wall. The true
outlet is at the point
the stomach wall

partial gastrectomy show that these stomachs do distend⁴ and roentgen studies show very well that the true outlet of the stomach is in fact the diameter of the distal loop of jejunum and not the entire circumference of the stomach (see Figs. 2 and 4). That portion of jejunum opposite the cut end of the stomach is then in actuality part of the stomach wall.

SUMMARY

A study of ninety patients who were subjected to partial gastrectomy for duodenal or gastric ulcers has led us to one obvious conclusion that is that the true gastric stoma is not the entire width of the remaining portion of the

stomach, but must of necessity be that narrowed outlet which leads into the jejunum. This outlet cannot be larger than the luminal diameter of the jejunum. Since this is so, great care must be exercised to avoid rotation of the jejunum onto the greater curvature of the stomach which would obstruct the true stoma. Regardless of the type of anastomosis performed, the size of the true gastric stoma remains the same. Roentgen studies show rather conclusively that with the passage of time the residual stomach and its jejunal lower wall dilates so that more food can be accommodated and the true stoma then behaves much like the pylorus. Ultimately a balance is reached so that these patients are able to eat a normal amount of food without discomfort.

CONCLUSIONS

- 1 The true gastric stoma is not the entire circumference of the residual stomach.
- 2 The true gastric stoma is only that narrowed jejunal diameter into which the stomach empties, and is found at the lower end of the anastomosis.
- 3 The size of the true gastric stoma remains the same regardless of the type of gastric resection performed.
- 4 With the passage of time, the jejunal wall of the stomach pouches outward and the residual stomach dilates so that the true gastric stoma becomes displaced to the left.
- 5 Roentgenograms taken four years postoperatively show that the true gastric stoma now behaves much like the pylorus with regard to peristaltic activity.

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CHOLECYSTECTOMY AND PARTIAL HEPATECTOMY FOR CARCINOMA OF THE GALL BLADDER WITH LOCAL LIVER EXTENSION

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RECENT advances in anesthesia, supportive intravenous therapy, and the easy availability of blood transfusion have greatly extended the scope for curative and palliative surgical procedures. Many operations previously considered impractical or too hazardous may now be undertaken not lightly, but certainly with the thought that a reasonable degree of success is to be anticipated.

This case is presented as another instance of partial hepatectomy and cholecystectomy for carcinoma of the gall bladder with metastasis grossly localized to the adjacent liver.

CASE REPORT

J. M., aged 61 years a barber, was admitted to the medical service of the Coner Island Hospital on Sept. 27, 1941. For fifteen months he had had recurring attacks of right upper abdominal colicky pain. He tolerated fatty foods poorly. There increased flatulence and a feeling of abdominal distention. There was a loss of sixty to seventy pounds in the year preceding hospital admission. Gall bladder studies indicated a nonfunctioning gall bladder.

Physical examination revealed a fairly well nourished man not acutely distressed who showed evidence of recent weight loss. Examination was essentially negative except for the local findings. On abdominal palpation a tender mass could be felt in the right upper abdomen. The liver edge was palpable two fingerbreadths below the costal margin and was sharp except where it merged with the mass which was interpreted as being gall bladder. There was moderate abdominal spasm. In the twelve day period of observation prior to operation a febrile course persisted. The temperature ranged from 100 to 100.2° F. Gall bladder x-ray series on Oct. 5, 1941 again revealed a nonfunctioning gall bladder. One large ring shaped shadow could be seen in the right upper quadrant. This had the appearance of a gallstone.

Laboratory data were as follows: hemoglobin, 5% per cent; white blood cells 9,500; Wassermann was negative; urine negative; blood sugar 101 mg. per 100 c.c. and urea 12 mg. per 100 c.c. The total blood protein was 6.6 Gm., albumin 3.9, globulin 2.6, cholesterol 194 mg. per 100 c.c., cholesterol esters 71 mg. per 100 c.c. and icterus index 5.

On Oct. 8, 1941 a laparotomy was performed under spinal anesthesia through a right upper rectus muscle splitting incision. The gall bladder was enlarged. The fundus was hard and had a peculiar whiteness to it. The entire distal two-thirds of the gall bladder was intimately fused with the overlying liver bed. The liver around the gall bladder bed contained numerous various sized nodules—obviously metastatic carcinomatous nodules. The involved area in the liver was localized to the region about the gall bladder. No other gross metastases could be seen. The glands in the porta hepatis were not enlarged. The gall bladder also contained numerous calculi. The proximal third, the neck and cystic ducts were free of neoplastic disease. The condition was apparently one of carcinoma of the fundus of the gall bladder with localized metastases to the surrounding liver. The cystic duct was isolated, clamped, cut, and ligated. The cystic vessels were ligated and cut. A series of deep mattress sutures was placed through the liver surrounding the grossly involved portion and tied. The

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Fig 1—Gall bladder and segment of excised liver, anterior aspect



Fig 2—Gall bladder and segment of excised liver, posterior aspect

involved liver lobe and attached gall bladder was then resected. Hemostasis was relatively easy to obtain. An occasional bleeding area was seen. This could be clamped and ligated readily. The surrounding deep sutures were effective and controlled most of the potential bleeding. After the segment of liver was removed, the liver gap was closed by approximating the cut surfaces by several deep sutures. A Penrose drain was placed down to the foramen of Winslow and the abdomen closed in layers. Postoperative recovery was uneventful except for some complicating bilateral pulmonary atelectasis which cleared spontaneously. The patient was discharged on Oct. 29, 1943 (twenty-fourth day postoperative) the wound well healed and symptom free.

Figs. 1 and 2 show the gall bladder and the segment of liver involved. Fig. 3 is a microphotograph of the lesion on an epidermoid carcinoma of the gall bladder.

When seen several months after operation the patient was relatively well. He then moved to another community, where he died approximately seven months postoperatively, presumably from recurrence, although the cause of death could not be ascertained.

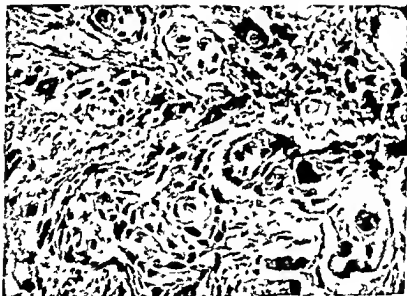


Fig. 3—Microphotograph epidermoid carcinoma of gall bladder (high power)

DISCUSSION

In 1891 Keen¹ excised an adenoma of bile ducts by Paquelin cautery and fingernail emulectomy. In 1897 he removed a liver angioma by extraperitoneal elastic constriction and in 1899 he excised the left lobe of the liver involved by carcinoma by Paquelin cautery. Hemorrhage was controlled by the cautery, digital compression, and suture ligation. All three patients recovered from the operation. Seventy-three other cases of partial hepatectomy for various causes were collected from the literature.

Thompson² successfully resected a gumma involving contiguous parts of the right and left liver lobes. He collected cases of liver resection and reported six deaths in forty-two cases.

CASE NO.	AUTHOR AND YEAR	NO OF CASES	PROCEDURE	RESULTS	
				IMMEDIATE AND ULTIMATE	FEMATICS
				Died from splenemia	Operative mortality
1	Quoted by Keen Kuester, 1892	1	Tumor exteriorized elastic liga- tures	Recurrence in 2 mo and death	Delayed operative mortality
2	Watson, 1896	1	Wither ligatures through normal liver tissue about the lesion allowed to slough out	Recurrence and death 6 mo later	Early recurrence
3	Ulman 1897	1	Excision of tumor of gall bladder, and resection of ductus hepat- icus liver stump extraperito- nealized	Death in 6 weeks	Delayed operative mortality
4	Wasservater 1897	1	Hemostatic silk sutures through liver substance thermocautery excision of gall bladder, and infiltrated portion of liver, iodoform gauze packing	Died of recurrence 8 mo later, early recurrence	These were 3 cases out of 35 cases of malignant disease of the liver and bile passages where surgery appeared feasible
5	Robson is 1894	3	(1) Exteriorized gall bladder and involved liver elastic ligatures about knitting needles	Died of recurrence 6 mo later, early recurrence	No liver enlargement at death, died of cachexia at 3 yr
6			(2) Exteriorized gall bladder and inver-elastic ligatures	Died of shock several hours post operatively, operation mortality	No follow up
7			(3) Case with numerous adhesions treated as first cases	3 yr survival, well 2 yr	
8	Quoted Hochberg (Vienna)	1	Removal of gall bladder and ad- joining liver for carcinoma	Patient well 1 weeks later, no further observation	
9	Monks, 1896	1	Excised gall bladder, liver seg- ment, and part of anterior wall of stomach	Operative recovery, died 2 mo postoperatively, details not known	Regional lymph nodes involved at original operation
10	Terner and Auvray 17 1900	1	Cholecystectomy and liver resec- tion (iodoform gauze packing of cut liver section)	Recurrence 7 mo postoperatively liver metastases, died 10 mo postoperative	
11	Quoted (1) Cerny, 1893	1	Cholecystectomy excision of meta- static nodule from liver paren- chyma	Operative recovery, no follow up	
12	(2) Cerny, 1898	1	Resection of liver and gall bladder for extensive growth of gall bladder infiltrating the liver	Operative recovery—no follow up	
13	(3) Duret, 1898	1	Resection of liver and gall bladder		
	(4) David Grieg, 1897	1			

(Continued on following pages)

TABLE I (CONT'D)

CASE NO.	AUTHOR AND YEAR	NO. OF CASES	PROCEDURE	RESULTS AND ULTIMATE	REMARKS
14	(a) Hildebrand 1896	1	Resection of liver and gall bladder	Recurred 3 mo postoperatively	
15	(b) Hildebrand 1896	1	Resection of liver and gall bladder	In good health 1 1/2 yr postopably—no follow up after that	
16 17	(7 & 8) Karsenz 1893	2	Resection of liver and gall bladder	No other information as to follow up operation to recovery but no follow up	
18	(9) Terrer 1890	1	Resection of liver and gall bladder (cryogenic lesion)	Operation recovered as usual's later evidence	
19	Mayo 1900	1	Gastroscopy and liver resection on resected common duct and portion of duodenum in addition	Early recurrence	
20	Garre 1903	1	Gastroscopy and edge shaped resection of liver related metastases excised separately	Recurred 6 (no not stated)	
21	Franklin 1913	1	Resection of gall bladder with edge of liver interposed omentum and sutured together	Recovery postoperative and clinically no postoperative	
22 23 24	Walton 1911	3	Jejunum related to large portion of liver was resected gall bladder	All 3 cases later recurrence in liver tumor or liver within a few months longest period of freedom as 6 mo	Operation really controlled
25 26 27	Monte 1930	1 1 1	Gastroscopy and resection of liver and gall bladder	Early recurrence Survived 6 mo later Well 6 1/2 yr later	
28	Gray 1934	1	Gall bladder and duodenum resection—about 2 cm of normal tissue all around excised tumor as a by electric coagulation and through multiple sutures	Remained recovered no follow up	100% incidence of recurrence of gall bladder in 300 patients on gall bladder or biliary tract

29	Hodberg and Kogut 23 1939	1					Patient well 14 mo later and gained 26 1/2 pounds	
30	J R Patena (personal communication to Mattson) 1942	1					Successful resection follow up not given	
31	Bolander 23 1943	1					One year later patient was well and had gained 20 pounds	
32	Collected from the Literature	1					Died 1 mo later	
33	Chaserni	1					Patient well 1 yr later	
34	Polizi	1					Patient died 1 yr later	
35	G oja	1					Patient still 3 mo later no further follow up	
36	Lambert	1					Well 3 mo postoperatively 1 1/2 years later cause unknown but presumably due to metastases	
37	Sheinfeld 1945	1					Excision of portion of liver with gall bladder to eliminate contiguous metastases	

TABLE II. CARCINOMA OF THE GALL BLADDER—CHOLECYSTOMA OR OTHER OPERATIONS

AUTHOR	DATE	NO. OF CASES (11 collected cases 17 where liver resection was done)	NO. OF PATIENTS OPERATED ON AND FOLLOWED (Cases where liver resection was done are excluded)	NO. OF CHOLECYSTOCTOMIES	REMARKS (THE MORE FAVORABLE CASES AFTER CHOLECYSTECTOMY) 3 cases as follows: No recurrence at 1½ yr., 7 yr., 26 mo., 2 yr., 1 yr. 1 died at 2½ yr.
Barnes	1911	21	— (11 explorations, 7 cholecystostomies, 1 gastroenterostomy)	1	2 alive at end of 4 yr.
Interdoni Quetaz Korte Werner Kammel Riegel	1912	1	1	1	1 early death Alive 5 yr later
Shelly & Hootes	1912	11	10	11	7 patients well after 3 yr
Vignas	1913	1	1 (also resected intestinal con- mon duct)	13	1 patient living 6½ yr (11 died within 2 weeks) Alive and well 7½ yr postoperatively
Brown & McFetridge	1916	23	19 (11 explorations, 1 cholecystostomy)	4	1 case with possible hope of survival— malignancy an incidental finding
Rhodes & Greenblatt	1917	21	22	5	1 patient alive and well after 5 yr

Cooper ²⁵	1937	48	45	16	1 alive and well ~ 3 yr, 25% mortality in cholecystectomy cases, 38% mortality in exploration; average duration of life 3½ mo
Lewis	1940	34 autopsies	33 (Explorations and biopsies, 1 cholecystectomy, 1)	9 (1 had radium in addition)	5 cholecystectomies appeared to have no metastases but 4 patients died in 10 mo from recurrence after cholecystectomy
Quéau & Masse ²⁶	1941	1	1	1	1 alive and well after 5 yr, lesion not suspected at operation
Greenlee, Hamilton, & Ferraris	1941	5	5	3	Survived 14 yr (bel of intercurrent ailment)
Mattson ²⁷	1942	60	No details		1 died at 13 mo (others died sooner)
Vadheim Gray, & Dockerty ²⁸	1944	77	54	44	No successful case
					7 alive and well 5 yr (4 more than 1 yr), grade 1
					1 survival 6 yr, (grade 2)
					1 died at 18 mo, (grade 4)
					3 died of other causes, 2 surviving 5 yr, (grade 1)
Finney & Johnson ²⁹	1945	18	18	3	1 died at 1½ mo, 1 at 25 mo

Garre³ in 1907 published six cases of liver resections for carcinoma, sarcoma and echinococcus disease.

In the *Proceedings of The Royal Society of Medicine*,⁴ 1922-1923 a symposium on partial hepatectomy was presented.

Grey Turner⁵ presented a case of an adenoma—a large lobulated tumor in the right lobe of the liver weighing two pounds and three ounces which he successfully resected. He quoted a case of Dr. George Hume. This was a liver resection for a large and localized liver recurrence of a stomach carcinoma. Death occurred twelve months later from further recurrence.

Philip Turner⁶ removed a bleeding adenoma by Paquelin cautery but the patient succumbed to shock in the immediate post-operative period.

A large primary carcinoma in the right lobe of the liver was excised together with the gall bladder by Wright. He stated that cutting boldly through the liver is safe. Hemorrhage can be controlled by hot packs and then picking up bleeding vessels. Other types of liver tumors and resections were presented.

Abel⁷ removed the entire left lobe for adenocarcinoma of bile duct origin. The specimen weighed five pounds. However there was recurrence nine months later.

The liver has been resected successfully in cases of direct invasion by carcinoma from a contiguous primary carcinoma as in carcinoma of the stomach, colon or kidney.

Cattell⁸ resected a large solitary metastasis of the liver at the first stage of a two-stage abdominoperineal resection for carcinoma of the rectum. The patient was well one year later.

Pickrell and Clay removed the left lobe three times in a four-month period for carcinoma, hemangioma and gumma.

Pickard and Stevenson⁹ reported the excision of a large hepatoma from the right lobe of a boy of 13 months.

Numerous instances of liver resection are present in the literature. Most of these were successfully performed. By correspondence Tinker and Tinker¹⁰ in 1939 collected fifty-nine instances of liver resections by members of the American Surgical Association. Most of these were presumably unpublished. This operation must undoubtedly have been performed many more times without publication. Very likely the unsuccessful cases were not reported. However there is an abundant literature now extant which illustrates that the majority of liver lesions suitable for excision may be excised whether in the right or left lobes even if not pedunculated without a prohibitive mortality or morbidity rate.

Regarding the specific problem presented by this case report the question of whether the procedure is worth while arises. Table I is a summary of 36 cases collected where the gall bladder and contiguous liver were excised for carcinoma and direct extension into the liver or localized liver metastasis. Immediate operative mortality was 5.5 per cent (2 cases), delayed operative mortality 8.3 per cent (3 cases), a total operative mortality of 13.8 per cent. Early recurrences occurred in 38.8 per cent (14 cases), 22.2 per cent (8 cases).

recurring within six months and 16.6 per cent (6 cases) between six months to a year. Good palliative or possible good long time results are noted in 19.4 per cent (7 cases). One patient died three years postoperatively of metastases; two patients were well one year postoperatively, three were well at 14, 15 and 18 months respectively, and one $6\frac{1}{2}$ years after operation. Twenty-two per cent or eight patients made operative recoveries but had no adequate follow up studies. One patient died one month and another six months postoperatively from possible unrelated causes. It must be remembered that these cases are collected from the literature and may form a selected group favoring the cases with relatively better results since those in which poor results were obtained may have remained unpublished. Nevertheless this group of cases merits consideration. The results compared with those cases where simple cholecystectomy, exploration with or without biopsy, or other less radical procedures upon the gall bladder and liver were done, are favorable.

Table II is a collection of reports of various series of gall bladder carcinoma and some single or small series case reports. Four hundred seventeen cases are collected. Two hundred eighty-four patients were operated upon. Cholecystectomy was performed 157 times. In twenty-eight cases there are possible good long time results: 9.8 per cent of the total number of patients operated upon or 6.7 per cent of the total number of cases collected. There are 16 five year, 3 four year, 4 three year, 3 two year, and 1 one year survivals alive and well at that time. The survival time is not mentioned of the other case placed in this category. Five patients (1.7 per cent of the patients operated upon) lived 30, 25, 18, 16 $\frac{1}{2}$, and 13 months respectively following operation. The remainder all succumbed within a relatively short time. Immediate operative mortality cannot be given from the data available. In Cooper's series it was 20 per cent. Walters and Snell¹² give it as 10 per cent. In evaluating the factors influencing survival time or recovery, Webber's¹⁴ work must be considered. In a study of thirty patients who had been subjected to cholecystectomy from the point of view of grade of malignancy, Broders' classification, he noted the following. Local extension and metastasis were considerably higher in grade 3 or higher carcinoma. The postoperative length of life was considerably better in the lower grades, less ones.

From a survey of these cases collected, liver resection where possible appears to be of definite palliative value. The results in general are, however, poor when compared with the results of radical surgery for carcinoma of other organs.

SUMMARY

A case of epidermoid carcinoma of the gall bladder with metastases localized to a resectible area of the liver is presented.

The feasibility and palliative value of liver resection for carcinoma of the gall bladder and local liver extension are discussed.

For comparison, the results obtained with cholecystectomy for early carcinoma or simple exploration and biopsy for more advanced carcinoma are given.

THE CAROTID SINUS SYNDROME ITS SURGICAL TREATMENT

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IN RECENT years many excellent contributions have appeared in the literature on the anatomy^{2, 3, 17, 20} and physiology^{1, 2, 4, 7, 9, 10, 22, 23} of the carotid sinus. In 1933 Weiss and Baker called attention to the significance of the carotid sinus reflex particularly in its abnormal phases in man.²² They presented evidence that an abnormally sensitive carotid sinus reflex could be responsible for the syndrome of spontaneous attacks of vertigo, syncope, and convulsion or milder manifestations. A number of observers have confirmed the existence of what has come to be known as the carotid sinus syndrome.^{11, 12, 14, 23} Many individuals with an abnormality of the carotid sinus reflex suffer only mild symptoms; however, there are a number of the more severely afflicted persons in whom the symptoms of dizziness, vertigo, and syncope may not only be dangerous but totally disabling. These patients have been afforded relief by surgical denervation of the carotid sinus. We wish to report three cases of carotid sinus syncope and to review briefly the significant aspects of the carotid sinus syndrome.

The carotid sinus syndrome of spontaneous attacks of dizziness and fainting occurs as a result of a hypersensitive state of the carotid sinus reflex. It results through one or more of three main reflex arcs. The afferent or sensory limb is probably always the same, but the motor pathways differ.

The carotid sinus is a small bulbous dilatation of the first part of the internal carotid artery. Its walls are supplied by a dense plexus of nerves and sensitive end organs, some of which appear to respond to stretch or pressure and others to chemical stimuli. Impulses which result from such stimuli arise in the carotid sinus and travel centrally to the medulla.⁹ The principal afferent pathway is by the carotid sinus nerve (nerve of Hering) which connects with the glossopharyngeal nerve, the vagus nerve, the cervical sympathetic chain, and occasionally the hypoglossal nerve.^{9, 17, 20} The three motor pathways responsible for syncope involve the vagus nerve, the vasomotor depressor nerves, or the central motor pathways, the clinical picture being determined by the efferent or motor pathways of the reflex.

The first or vagal type carotid sinus reflex is characterized by bradycardia, asystole, cardiac arrhythmia, hypotension, and finally cerebral anoxemia which may lead to convulsions or unconsciousness. The second or depressor type is characterized mainly by vasodilatation and a fall in blood pressure. Cardiac arrhythmia is not present but there may be cerebral anoxemia with resulting unconsciousness or convulsions. This is the least common and usually accompanies one of the other two types. The third or cerebral type is characterized by sudden unconsciousness with no change in pulse rate or blood pressure and

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without intervening symptoms. Commonly, a mixed type is present, the type of syncope being classified according to the dominant motor pathway involved.² The vagal type of sinus syncope can be prevented by the administration of atropine which paralyzes the vagal endings, or by epinephrine through its local stimulating effect on the ventricles. The depressor type of reaction is abolished by epinephrine through its constricting action on the small blood vessels. Anesthesia of the carotid sinus induced by procaine hydrochloride or surgical denervation of the carotid sinus will abolish an abnormal response of any of the three types.

In a normal person the mechanical stimulation of the carotid sinus does not produce symptoms. In a patient in whom the carotid sinus is abnormally sensitive, mechanical or chemical stimulation results in many symptoms as well as a specific effect on the blood pressure. Such patients complain of sudden attacks of dizziness and unconsciousness with or, more rarely, without convulsions.²² These attacks may occur without warning but are usually preceded by a definite aura which consists of weakness, dizziness, blurring of vision, and epigastric distress, the patient feeling as though he were going to faint. Such syncopeal attacks are usually associated with hyperpnea, pallor, perspiration, often profuse, falling convulsive movements, declining blood pressure, slowing of the cardiac rate and cardiac arrhythmia. Unconsciousness may last a few seconds to a few minutes, recovery, however, is usually prompt. The frequency and severity of the attacks vary greatly, even in the same person. The precipitating factors cannot always be discovered but often attacks result from turning the head suddenly, stooping, looking up, pressure on the sinus in resting the head on one hand, wearing a tight collar, or changing the position of the body quickly. Fatigue, emotional upsets and menstruation may precipitate the symptoms. In many cases, however, no cause can be found. Symptoms almost always occur when the patient is in the upright position. Carotid sinus syncope is more common in middle aged and elderly persons, however, it occurs rarely in young people. Not infrequently it is associated with such disorders as arteriosclerosis, hypertension, emotional instability, syphilis, cervical lymph adenopathy and digitalis intoxication.²³

The diagnosis²⁴ of hyperactive carotid sinus is made from the history and by inducing an attack of syncope by making digital pressure over the carotid sinus with the patient in the upright position. Both sinuses should not be stimulated simultaneously. Infiltration of the region of the sinus with 1 per cent procaine will abolish an induced attack and also prevent the reproduction of an attack by mechanical stimulation, thus serving to distinguish true attacks from hysteroneurosis. At the time of manipulation changes in the pulse rate, blood pressure and if possible the electrocardiogram should be recorded. One side is always more sensitive than the other. It is important that as far as possible the patient be classified as to type, vagal pressor or cerebral. Carotid sinus syncope may simulate atypical petit mal, grand mal, Ménière's disease, hysteria, narcoleptic or cataleptic seizures, however these attacks cannot be induced by stimulation of the carotid sinus.

CASE REPORTS

CASE 1—A housewife, aged 59 years, was seen in the Clinic in February, 1933, complaining of recurrent attacks of syncope for fifteen years. At first the attacks were infrequent and were characterized by "feeling weak," "a sensation of everything turning dark," and loss of consciousness. They were of two to ten minutes' duration and occurred only when she was in the upright position. There was no biting of the tongue, incontinence, or convulsions. They were not precipitated by any specific movement, however, they occurred more frequently during menstruation and at the time of the menopause. During the previous year the syncope attacks had occurred with increasing frequency and severity and without warning. Two weeks prior to examination she had fallen in the bathroom during an attack and lacerated her scalp badly.

Physical examination revealed moderately generalized arteriosclerosis. The heart was not enlarged. Blood pressure was 142 mm systolic and 74 mm diastolic, the pulse rate 70. Laboratory studies of the blood and urine, including a blood sugar and serum calcium, were within normal limits. The electrocardiogram was essentially normal.

Pressure over the right carotid sinus caused no essential change in the blood pressure, cardiac rate or state of consciousness. Pressure over the left carotid sinus caused a marked drop in blood pressure, slowing of the pulse rate and syncope. Denervation of the left carotid sinus was done March 10, 1933. She was discharged improved on March 15, 1933.

The patient was last seen May 15, 1937, four years and two months following operation. There had been no fainting since operation. She complained of an occasional attack of pain in the face, beginning in the nose and spreading over the head. Except for slight ptosis of the left eye and slight swelling about the ear, examination gave negative results. Blood pressure was 155 mm systolic and 85 mm diastolic. No changes could be induced by pressure on the carotid sinus.

CASE 2—A housewife, aged 61 years, was seen in the Clinic in June, 1939, complaining of rectal bleeding and constipation of one year's duration. Examination revealed carcinoma of the rectum. On June 15, 1939 an abdominoperineal resection was done. Conalescence was uneventful. She gained weight and strength and managed the colostomy well.

The patient returned to the Clinic in January, 1942, complaining of dizziness and syncope. For many years she had had attacks of dizziness but not until the past three years had they been associated with falling and syncope. She had suddenly become dizzy, lost consciousness and had fallen several times during the past year. Within the last two months

She was aware that turning the head do with precipitating the attacks. Medical measures. She had no complaints suggestive of recurrent malignant disease.

Examination revealed the patient to be well developed, with a functioning colostomy. A moderate degree of arteriosclerosis was present. The heart was not enlarged. A small suprascapular lipoma was present on the right side of the neck. Blood pressure was 150 mm systolic and 85 mm diastolic, the cardiac rate was 80. Laboratory studies of the blood and urine gave negative results. The electrocardiogram was essentially normal.

Pressure over the right carotid sinus caused no change in the blood pressure or cardiac rate. Pressure over the left carotid sinus caused marked slowing of the pulse, asystole for four seconds, a fall in blood pressure, vertigo, and syncope. Excision of the right suprascapular lipoma and denervation of the left carotid sinus was carried out on Feb. 1, 1942.

During a four year follow up there has been no return of the spontaneous attacks of dizziness and syncope. Carcinoma of the ala of the nose developed which was treated by irradiation. Later, a plastic operation was done on the nose. The patient was last seen March 15, 1946, at which time she was quite well except for moderate nervousness and weakness. There was no evidence of recurrence five years and nine months after abdominoperineal resection for carcinoma of the rectum. No change in blood pressure, cardiac rate, or consciousness could be elicited by pressure over the carotid sinuses. Blood pressure was 155 mm. systolic and 90 mm diastolic.

Case 3—A 51 year old, married, white man, a cab driver, was admitted to the Clinic on Nov. 1, 1942, complaining of attacks of dizziness and unconsciousness. He had been well until one year prior to his visit to the Clinic, at which time he had the first attack of dizziness and sudden unconsciousness. He was of a nervous disposition and during the past year had three attacks of dizziness and sudden unconsciousness. He could not associate the first two attacks with any particular movement but was certain the last one was associated with turning the head to the left quickly. While driving the cab he started to turn around at an intersection, as he looked backward over the left shoulder, he suddenly became unconscious and the cab ran into a pole. There was no incontinence, biting of the tongue, or convulsions. He recovered shortly and was taken to an emergency hospital where similar attacks of unconsciousness were reproduced by "pressure over the left side of the neck." He was not permitted to return to work. After a brief but unsuccessful trial with medical therapy he was advised by his physician to have surgical treatment.

Examination gave essentially negative results. The heart was not enlarged. The blood pressure was 110 mm systolic and 70 mm diastolic, the pulse rate was 70. Laboratory studies of the blood and urine, including serum calcium and blood sugar determinations, were negative. The electrocardiogram was normal.

Pressure over the right carotid sinus resulted in slight change in blood pressure and cardiac rate. Pressure over the left carotid sinus caused a marked fall in blood pressure, slowing of the cardiac rate, pallor, dizziness, and unconsciousness. On Dec. 1, 1942, the left carotid sinus was denervated. He was discharged on the fifth postoperative day improved.

On the night of discharge from the hospital, the patient attended the theater and did not return home until late. The following morning while shaving, he had a spontaneous attack of dizziness and unconsciousness. He fell to the floor but did not injure himself. His wife stated that when she reached him he was pale and perspiring, but was having no convulsive movements. There was no incontinence or biting of the tongue. He regained consciousness in about four minutes but was disoriented and not aware of what had happened. Examination on the following day at the Clinic gave negative results. The incision over the left side of the neck was healing per primam. Compression of the carotid sinus on either side did not result in syncope. When the history was reviewed, he admitted, for the first time, that some thirty years before, when he was 19 years of age, he had a seizure during which he lost consciousness for a few minutes. He denied any attacks of vertigo, syncope, or convulsions during the thirty one year interval between this seizure and the onset of the present illness. He was referred to the neurologic department for further study. Roentgenologic studies of the skull were negative. An electroencephalogram was done at the Boston Psychopathic Hospital and reported as follows: abnormal encephalographic report—verbal consistent with vulnerable cortex and epileptic dysrhythmias. Neurologic examination was negative except that he was apprehensive and nervous. The neurologist believed that he was not an epileptic and that he did not have a brain tumor. Because of the nervousness he was placed on small doses of phenol trinital daily. After a short period of observation he was permitted to return to his job as a cab driver.

The patient was last seen May 10, 1944 eighteen months following operation, at which time he was feeling well except for nervousness and an occasional attack of dizziness. There had been no syncope, unconsciousness, or convulsions. No changes could be elicited by pressure over the carotid sinuses. Blood pressure was 130 mm systolic and 82 mm diastolic.

COMMENT

Case 3 is particularly interesting. In view of the rather atypical history and seizures, the patient was not considered to be an epileptic. Robinson¹³ has made an interesting study to determine the incidence of hypersensitive carotid sinus reflex among 1,000 cooperative institutional patients with epilepsy. In every instance, syncope, convulsions, or transitory loss of consciousness had brought the patient to the hospital. Of the 1,000 patients examined 9 had a

hypersensitive carotid sinus reflex, an incidence of 0.9 per cent. In five cases a hyperirritable reflex seemed to be the sole mechanism underlying all seizures—spontaneous and induced. Three patients had hyperactive carotid sinus reflexes and were also known to have an additional convulsive mechanism.

The anesthetic management of the hyperactive carotid sinus has been well presented by Rovenstine and Cullen¹⁴ and Ruzicka and Eversole.¹⁵ Although this discussion pertains primarily to the surgical treatment of the hypersensitive carotid sinus, the surgeon as well as the anesthetist should be aware of the reactions that may occur from an apparently normal sinus which has been sensitized.^{6, 12} It should be emphasized that an apparently normal carotid sinus may be sensitized by various drugs^{6, 7} (morphine, digitalis, thyroid extract), anesthetic agent^{14, 21} (light anesthesia, nitrous oxide, cyclopal), or surgical procedure²¹ (operation on the neck). During an operation a patient without previous evidence of an abnormal carotid sinus may suddenly exhibit alarming signs such as pallor, bradycardia, arrhythmia, asystole, hypotension, and apnea. Reactions occur most often during operations on the neck and death may result suddenly. Such deaths are often said to be the result of circulatory failure. When such a carotid sinus reaction occurs, treatment must be started immediately. The head should be lowered, oxygen administered, packs and retractors removed, and 3 to 5 cc. of a 2 per cent solution of procaine hydrochloride infiltrated at the area of the bifurcation of the common carotid artery.²⁴ Stimulants and fluids are of no value.

In a study of the surgical anatomy of the carotid sinus, Sheehan, Mulholland, and Shafiroff¹⁷ found that the principal nerve supply to the sinus was through the glossopharyngeal nerve by way of the carotid sinus nerve (nerve of Hering). They concluded that "the anatomy suggests the feasibility of dividing the carotid sinus nerve in preference to extensive stripping of the carotid artery in the surgical treatment of carotid sinus syncope." It has also been shown by Code, Dingle, and Moonhouse⁴ that the cardiovascular components of the sinus reflex are conducted solely through the carotid sinus nerve. Ray and Stewart's observations however indicate that the glossopharyngeal nerve in man is not in every instance the only nerve through which afferent impulses of the carotid sinus reflex are transmitted. Anatomically, it may be feasible to section only the carotid sinus nerve in the treatment of carotid sinus syncope. We believe that the surest way of denervating the sinus is by section of the carotid sinus nerve and extensive stripping of the common internal and external carotid arteries. Immediately after denervation of the sinus an increase in the blood pressure and heart rate occurs. This is only transient²² and it has been shown that in man hypertension and tachycardia following even bilateral denervation rarely last as long as a week.⁸

Treatment of the carotid sinus syndrome may be medical or surgical. Those patients in whom the symptoms are mild and the attacks occur infrequently may require no treatment as they can be managed by reassurance and conservative measures. If possible, fatigue, worry, and emotional upsets should be eliminated. They should be advised to avoid turning the head quickly,

looking upward, or stooping suddenly. Any constriction about the neck should be avoided. Should the attacks, even though mild, occur with increasing frequency, medical treatment should be instituted. Many drugs have been used—phenobarbital, ephedrine, atropine, benzedrine, and so forth—but have not been particularly satisfactory.^{5, 12} A number of patients may be helped by excision of inflammatory or neoplastic cervical glands, by antisyphilitic therapy, or by diminishing the dose in digitalis therapy. Stevenson¹⁰ has suggested x-ray irradiation of the carotid sinus as suitable treatment for the hypersensitive reflex. We have had no experience with this form of treatment. Surgical treatment is indicated in (1) those patients in whom the symptoms are severe and incapacitating, thus preventing them from carrying out their usual occupation; (2) those in whom medical therapy has been unsuccessful either because of poor response to medication or because of drug intolerance, and (3) usually those in whom the mixed or cerebral type of response is presented.

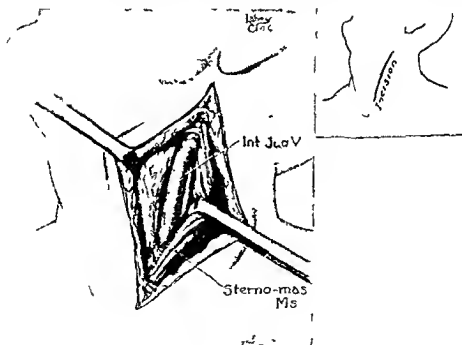


Fig 1.—The sternomastoid muscle has been retracted laterally and the carotid sheath opened exposing the internal jugular vein. Insert shows location of incision.

The operation consists of stripping the common internal and external carotid arteries at the bifurcation, sectioning the carotid sinus nerve, and removing the intercarotid tissue. Endotracheal cyclopropane and ether anesthesia are recommended. These may be supplemented by procaine block in the very hyperactive carotid sinus to prevent serious disturbances in pulse and blood pressure.

With the patient in the supine position the head is rotated laterally and the neck slightly extended exposing the side to be operated upon. The skin is prepared and the neck draped in the usual manner. An incision 8 cm long is made along the anterior border of the sternomastoid muscle centered at the level of the upper border of the thyroid cartilage (Fig 1). The incision

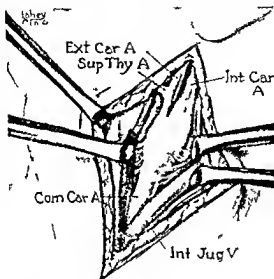


Fig 2—The dissection is continued and the internal jugular vein freed and retracted laterally with the sternomastoid muscle exposing the carotid sinus, the common, internal and external carotid and superior thyroid arteries.



Fig 3—The common internal and external carotid arteries have been completely freed. The carotid sinus is identified by perarterial stripping of the adventitia (see text). Insert a and b. The perarterial stripping is started below and carried well above the bifurcation of the common carotid artery.

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THE TREATMENT OF CAUSALGIA ARISING FROM GUNSHOT WOUNDS OF THE PERIPHERAL NERVES

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THE development of intractable pain and trophic disturbances following gunshot wounds of the extremities particularly those involving the peripheral nerves has long been recognized. To this syndrome the term *causalgia* was applied by Mitchell, Morehouse, and Keen¹ in 1864. By the use of this term, attention was called to the "burning" character of the pain of which the patient frequently complained.

The incidence of this condition is expectedly greater in time of war when so many casualties with wounds of the sensitive structures come under observation. Spiegel and Milowsky² described in detail nine individuals observed in a series of 275 cases of unselected peripheral nerve injuries. Mayfield and Devine³ encountered fifteen cases of severe *causalgia* in a group of 737 peripheral nerve injuries, an incidence of 2 per cent. In civilian life this condition is not rare. Miller and de Takats⁴ have emphasized the frequency with which some form of *causalgia* like pain may be observed in all injuries.

Early recognition of *causalgia* is important not only because there are now available means of giving relief of the pain but especially because if this condition is allowed to continue severe and crippling deformities may result.

The characteristic feature of *causalgia* which serves to differentiate it from other forms of pain is that it always responds dramatically, even if only temporarily, to the interruption of the nervous pathways which course through the sympathetic ganglia supplying the segment. There are other features such as disturbances in sensation, deep pressure pain especially in the muscles of the extremity, reflex paralysis, *dyskinesia* on attempting voluntary movements of the part and the visomotor and trophic disturbances but these accessory observations are not uniform. The single constant finding is the response of the pain to the injection of procaine into the region of the paravertebral sympathetic ganglia.

Many theories have been advanced to explain the mechanism of this pain. According to Leriche⁵ the afferent pathway is through the sympathetic fibers both those contained in the mixed nerves and those in the perivascular nerve plexus. Laboratory investigations in the main have failed to demonstrate the presence of afferent fibers from the extremities in the sympathetic nerves or ganglia although Kuntz and his associates^{6, 7} have reported evidence both anatomic and physiologic of the presence of such sensory pathways in the experimental animal. Pereira⁸ has recently presented additional evidence that affer-

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ent fibers from the perivascular plexus in man traverse the sympathetic ganglia Lewis⁹ has advanced the concept that efferent discharges of sympathetic impulses produce anoxia through vasoconstriction and that the afferent pathway is mediated through a set of hypothetical 'nocifensor' nerves. This explanation simply acknowledges the fact that increased sympathetic activity is frequently observed and that blocking the sympathetic nerves relieves the pain but fails to identify the essential afferent mechanism. According to Livingston,¹⁰ the dysfunction of the sympathetic nerves is but one part of a more profound alteration of the physiologic status of the spinal cord centers.

Recent experimental work of Grant Leksell and Skoglund¹¹ has demonstrated that an artificial synapse is produced in a mixed nerve by injury or pressure. In the presence of such a zone of localized trauma centrifugal impulses give rise to centripetal action currents. They suggested that these findings might be of significance in explaining the mechanism of certain obscure types of pain. Doupe Cullen and Chance¹² have used this concept to explain the production of causalgia. In a series of patients who were carefully studied they showed that the pain was aggravated by any stimulus which called forth activity of sympathetic nerves and that it was ameliorated by conditions in which sympathetic activity was inhibited. According to their observations efferent discharges over sympathetic pathways traversed the artificial synapse at the site of injury and in this way produced impulses in afferent nerves which resulted in the sensation of pain. They also confirmed an observation originally made by Tinel³ that relief of pain in certain cases of causalgia might be produced by blocking the nerve distal to the point of injury. On the basis of the presence or absence of relief from suppression of impulses in the peripheral region of the nerve they classified their cases into the 'distal' and 'proximal' causalgic syndrome.

The present communication is based on a study carried on over a period of fourteen months of 114 cases in which the diagnosis of causalgia was made. These cases were selected on the basis of diagnostic tests from 2,167 casualties with wounds of the extremities; an incidence of approximately 5 per cent. In only twenty of these cases, however, was the causalgia classified as severe. The patients were Chinese soldiers who were cared for in a U. S. Army General Hospital. The casualties were received by air evacuation usually two to three days after they had been wounded. Their injuries had generally been treated in the forward area by debridement and plaster fixation at one of the portable surgical units or field hospitals. The patients were admitted to the general surgical service and these observations on causalgia were made during the day-by-day surgical management of the cases.

The Chinese soldier is especially suited to a study of subjective sensations. He is generally intelligent and cooperative. He is rarely neurotic. Although brave and accustomed to enduring hardships and privations he is not hesitant to show by word, facial expression and gesture that he is suffering pain. Above all it is not part of his philosophy to minimize his complaints even to gratify the medical officer who is caring for him and to whom he may be sincerely at

tached. The language barrier is if anything a help in arriving at an impartial evaluation of the results of treatment since the interpreter assumes the post of middleman venerated by centuries of tradition as an impartial judge.

Because of modern methods of treatment of wounds in the forward areas by excision of devitalized tissues and immobilization together with chemotherapy casualties are generally free from pain after the first few days unless infection or tissue ischemia are present. Passive movement of the extremities should not cause pain unless such a manipulation directly disturbs the injured tissues. Those patients should be suspected of causalgia whose complaints are out of proportion to the severity of their wounds, especially if the pain is greatly increased by passive movement.

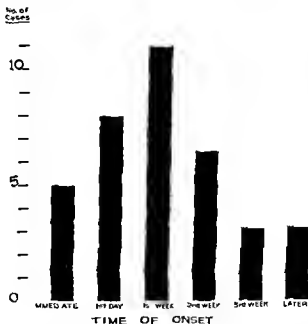


FIG. 1

Character of Pain—Although the pain of causalgia is characteristically described as burning in quality, out of a series of forty-two patients who were specifically asked to characterize their pain only seven applied this term to it. Thirty-one described it as numb in character and an additional four as 'sticking' or 'stabbing'. The pain was generally worse at night. Only four patients claimed that it was worse in the daytime. In two thirds of the group the symptoms were increased by wet weather but there was no significant change noted with variation in temperature.

Onset—In Fig. 1 the time of onset of the pain is analyzed. In a few patients the pain came on immediately after injury; in a larger number within the first day. The majority of patients developed pain during the first week.

and the incidence then decreased. It was interesting to note that in two patients the characteristic pain did not come on until as long as six weeks after the initial injury.

Examination—The diagnosis of causalgia in the severe case can frequently be made at first glance. Fig. 2 illustrates the typical appearance of the patient suffering from severe causalgia. The face is drawn with pain and the affected part zealously guarded from any movement or stimulation.



Fig. 2

(Courtesy of Museum and Medical Arts Service U. S. Army Medical Museum)

The patient's entire attention is absorbed by the pain and he is indifferent to surroundings. Any movement jarring of the bed or even noise produces aggravation of the pain so that he is in constant misery. Only five patients in the present series kept the hand wrapped in a wet cloth but frequently the patients shielded the extremities with bedclothes or garments. Voluntary movements of the extremity were effected slowly and with a curious jerking quality suggesting disinertia. Passive movements even when performed slowly, were associated with sudden muscular resistances. The muscles however, did not feel to be in spasm. Sensory examination revealed diffuse hypoesthesia and hyperalgesia which frequently spread far beyond the anatomic region of the injured nerve. Deep pressure especially of the muscles was painful.

Vasomotor and Trophic Disturbances—Early in the course, vasomotor changes were quite variable. Skin temperature and oscillographic readings were usually within normal limits. Only after weeks did the characteristic trophic changes occur. These abnormalities generally consisted in thickening of the skin with piling up of the epidermis, long hair, and atrophic nails. These disturbances appeared to be due chiefly to lack of use. Of more serious significance were the soft tissue changes especially about the joints of the hand. With prolonged pain and immobilization these joints became so stiff that the hand was frequently useless even when the pain had subsided. It was my experience that the Chinese soldier was generally not benefited by even the most painstaking treatment in the physiotherapy department. If movement caused pain, he just refused to move the affected part. The results were necessarily discouraging but furnished an even greater stimulus toward devising some form of treatment which by abolishing the pain, would allow the individual to use the part.

Paravertebral Injection of Procaine—The diagnosis was confirmed in every case by the clinical response to temporary interruption of nervous impulses traversing the sympathetic ganglia. For the lower extremity, 20 cc of 2 per cent procaine containing 2 drops of 1:1,000 adrenalin were injected into the region of the second lumbar ganglion. With the patient lying on his side a four inch No. 22 gauge needle was inserted through the skin in the depression between the lower border of the twelfth rib and the paravertebral muscles. The needle was advanced at a 60 degree angle from the horizontal using small amounts of $\frac{1}{2}$ per cent procaine to infiltrate the superficial tissues until contact was made with the body of the vertebra. The point of the needle was then advanced by successively withdrawing and depressing the hub during reinsertion until the point could be felt just gliding past the anterolateral surface of the lumbar vertebra. With the needle in contact with bone the solution was slowly injected.

For the upper extremity 15 cc of the procaine solution was injected by the anterior approach. With the patient recumbent and the head turned to the opposite side the scalenus anticus muscle was defined by palpation just lateral to the clavicular head of the sternocleidomastoid muscle. A point one inch above the clavicle was marked. After the skin and deeper tissues were infiltrated a No. 22 gauge needle $2\frac{1}{2}$ to 3 inches long was inserted at a 45 degree angle between the horizontal sagittal and the sagittal coronal planes of the body. At a depth of $1\frac{1}{2}$ to 2 inches contact was made with bone. Five cubic centimeters of solution were slowly injected. With rapid rates of injection serious reactions have been observed. The needle was then partially withdrawn and again inserted slightly caudadward so as to have the point pass over the head of the first rib. When once more in contact with bone 10 cc of the procaine solution were injected. In this series of cases 211 paravertebral injections of procaine were given. A pneumothorax developed in five patients although in only one case was it necessary to aspirate the air from the chest. There were no other serious reactions. Because of fatalities which have been reported during the injection of procaine into the paravertebral region it is necessary to re-emphasize the fact that the procaine must be injected slowly. The rate of injection should never

exceed 5 c c in one minute. Within five or at most ten minutes signs of paralysis of the sympathetic nerves should be apparent. Flushing of the skin, dilatation of the veins, and cessation of sweating are generally observed in that order. Increased warmth from arterial dilatation is slower in coming on. In addition, Horner's sign should be present when the thoracic ganglia are blocked.

The pain of causalgia frequently disappears even before signs of sympathetic paralysis are observed. With the cessation of pain the ability to move the part is increased. The deep muscle tenderness usually persists and pain is evoked on any attempt to manipulate stiffened joints. But the striking feature of causalgia is the disappearance of the pain even though the sensory and motor nerves are unaffected by the injection. This relief may last only as long as the effect of the procaine or it may persist for hours and even days. In the mild cases the pain may be permanently relieved by one or more injections.

TABLE I

UPPER EXTREMITY		LOWER EXTREMITY	
Brachial plexus	11	Sciatic	5
Median	15	Posterior tibial	6
Radial	18	Peroneal	5
Ulnar	13	Cutaneous	2
Cutaneous	3	Foot	3
Digital	2	Joints	1
Blood vessels	3		
Joints	4		
Total	52		23
Total cases	114		

Structures Involved—Causalgia has been reported most frequently after lesions of the median and sciatic nerves. In Table I is presented an analysis of the structures involved in this series of cases. This condition may apparently come on after injury to any sensitive structure. The severe cases, however, were seen only after injury of the brachial plexus, median, radial and ulnar nerves and in the lower extremity the sciatic nerve. Contusion or incomplete severance of the nerve was generally found when the lesion involved one of the major nerves. Pain following hand injuries which could be benefited by paravertebral procaine injection was frequently associated with complete division of one of the digital nerves.

TREATMENT

Since such striking relief was obtained from temporary interruption of the nerve impulses traversing the sympathetic ganglia and since lasting relief has been reported by Homans¹⁴ with repeated injections this form of therapy was first tried. It was disappointing to find that only mild cases of causalgia responded to one or even repeated injections. Even though there was temporary improvement relief did not persist. As many as eight injections were given in a single case without permanent benefit.

Preganglionic sympathectomy was then used for pain in the upper extremity in two patients. The sympathetic chain was divided below the third thoracic ganglion and the connections between the second and third ganglia and

the spinal cord were severed. Prompt relief was observed but within one week the characteristic pain had returned. Although not as severe as before sympathectomy it still prevented full use of the hand and above all soft tissue changes were not prevented.

On the basis that preganglionic section of the sympathetic supply to the upper extremity might not sever all the connections which were responsible for the development of pain resection of the ganglia including the stellate was then performed in four cases. Although the results were excellent in two cases only moderate improvement was obtained in the third case and in one patient although immediately after operation he was completely relieved within one week there was definite recurrence of the pain. Clearly, some other form of treatment was needed.

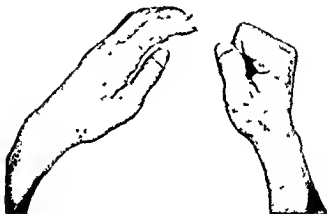


Fig. 3

(Courtesy of Museum and Medical Art Service U. S. Army Medical Museum)

It was noted at this time that the symptoms of causalgia were more effectively relieved by injection in those cases in which the extremity had been immobilized in plaster because of a coexistent fracture. Twenty-one patients were accordingly treated by immobilization in plaster with repeated paravertebral injections of procaine. Only ten of them obtained lasting relief and these were generally mild cases of causalgia. The end results as far as function were concerned were poor. Many of the patients developed marked soft tissue changes in their hands with stiffening of the joints of the fingers. Fig. 3 illustrates the useless hand produced by long standing pain and disuse.

On the basis that Leriche had obtained encouraging results in the treatment of causalgia from periarterial sympathectomy a more radical type of operation was used. Through the anterior supraclavicular approach the stellate second and third thoracic ganglia with the intervening chain were resected and in addition the adventitia with its plexus of nerves was stripped from the subclavian artery. This operation was followed by consistent relief of pain. It was used at first only in the long standing intractable cases in which all other forms

of treatment had been attempted. Seven patients who had had severe pain for from three to six months were subjected to this radical operation. Although the pain was relieved in each case in only two was there recovery of function. In the other five, although the pain was relieved, the soft tissue changes associated with months of disuse precluded normal function. Fig 4 illustrates the type of useless hand so often encountered. It is significant that no patient in whom the diagnosis of moderate or severe causalgia was made during the first part of this study was returned to duty.

A casualty was admitted to the ward in July, 1944, who had sustained a partial lesion of the brachial plexus from a shell fragment. He was suffering such intense pain that radical sympathectomy appeared to be the only form of treatment which would give lasting relief. He was operated upon ten days after the initial injury. Upper thoracic ganglionectomy and periarterial sympathectomy of the subclavian artery were performed. Not only was the pain permanently relieved but he did not develop any of the secondary changes of fibrosis, thickening of the skin or contractures. Fig 5 shows the flexibility of his soft tissues.



Fig 4

(Courtesy of Museum and Medical Arts Service, U. S. Army Medical Museum.)

In the succeeding ten cases of moderately severe and severe causalgia, paravertebral injection of procaine was used for diagnostic purposes only. The patient was then subjected to early radical sympathectomy. Relief of pain was obtained in all cases. The functional results were excellent. Crippling deformities from contractures and soft tissue changes were prevented. It is significant that of the ten patients treated by early radical sympathectomy, eight were returned to light duty. Even though the paralyses associated with the nerve lesions persisted, the patients had no pain and had free movement of the extremities.

There still remained the lesion of the peripheral nerve which required treatment for restoration of function. According to the prevailing opinion at

the time the earlier cases were being studied, suture or lysis of the peripheral nerve had been delayed until healing of the wound was complete. The report of Churchill,¹⁵ however, indicated that, with the use of penicillin, early secondary closure of wounds could be undertaken. Provided that no devitalized tissue or infection was present the wounds could best be closed between the fourth and tenth day after injury. This reparative surgery offered an ideal opportunity for removing the initiating factor which was producing the causalgia, namely, the irritation of the injured nerve.

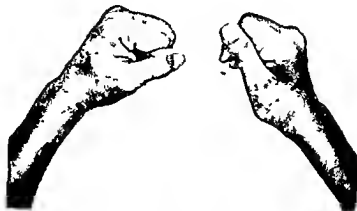


Fig 5

(Courtesy of Museum and Medical Arts Service U S Army Medical Museum.)

Four patients with causalgia were treated by this method. They were all suffering severe pain. The diagnosis of causalgia was confirmed by the temporary relief afforded by paravertebral injection of procaine either before or after operation. Penicillin, by the intramuscular route, was administered, 15 000 units every three hours, starting the day before operation and continued for three days afterward. In the operating room the fresh wounds were widely opened, all devitalized tissues excised, and the injured nerves sutured. The wounds were closed without drainage. Postoperative injections of procaine into the region of the sympathetic ganglia were needed in only two of the cases. After wound healing complete freedom of movement was preserved in each of the cases without the development of any fibrosis or soft tissue changes about the joints.

CASE REPORTS

CASE 1 (15937)—The patient was a Chinese soldier who sustained a perforating wound of the right wrist from a rifle bullet on Feb 3, 1945. Débridement of the wound with immobilization in plaster had been performed in the forward area. At the time of admission, four days later, he was suffering from severe pain in the hand and this pain was increased by any form of stimulation. Beginning flexion contracture of the fingers was already apparent and any attempt at passive movement was associated with severe pain. Paravertebral injection of procaine was followed by dramatic relief of pain which lasted for three hours. Nine days after injury he was taken to the operating room and, under anesthesia the plaster cast

the joint. Immediate primary suture of the wound had been performed in the forward area. The operative note which accompanied the patient stated that a suture of the divided ulnar nerve had been performed. At the time of admission on March 5 the wound was clean and the skin healed. The stitches had been removed before admission. The patient complained of severe pain and there was already a beginning flexion contracture of the fingers. Temporary relief was afforded by paravertebral injection of procaine. The following day he was anesthetized and the healing wound was widely opened. An anomaly of the ulnar nerve was disclosed in that the nerve was found to divide approximately three inches above the wrist. Only one of the divisions had been sutured and the nerve at this point was adherent with plastic exudate to the elemanous muscle and fascia. The vitalized portions were excised and the fresh ends of the two nerves were approximated. The wound was resutured without drainage and the wrist maintained in acute flexion with a posterior plaster splint. Complete and permanent relief of pain was afforded.

DISCUSSION

Recently published studies^{2,3} on the cases of causalgia resulting from gunshot wounds of the nerves incurred in World War II have come from general hospitals in the Zone of the Interior. The incidence of severe causalgia in nerve injuries has been given as from 2 to 3 per cent. In the present series the incidence in 2167 unselected cases of gunshot wounds of the extremities was 5 per cent although the severe cases amounted to less than 1 per cent. It is probable that the pain in many of the milder cases included in this study would have subsided spontaneously. It was only because an active search was made for cases of pain that were amenable to relief by blocking the sympathetic nerves that as large a group was found. Miller and de Takats⁴ have reported a similar high incidence of causalgia here pain after injuries in civilian life. It is likely that an even larger percentage of cases of trauma would have a causalgic component to the pain if appropriate studies were made.

A considerable period of time generally lapses between the initial injury and the time that the casualty arrives in a hospital in the Zone of the Interior in which definitive surgery can be carried on and completed. Although numerous studies have been carried out on patients who have had the pain for some months and in whom trophic changes and fibrosis of the soft tissues have already taken place, it is believed that the present series of cases is unusual in that the casualties were observed shortly after they had received the injuries and before the secondary changes could take place. An opportunity was thus afforded of instituting treatment at the earliest possible moment in order to prevent the development of irreversible damage to the soft parts. In addition daily contact with the patient during the period immediately after wounding, observation of the effects of treatment on the pain and above all the opportunity of inspecting at the operating table the fresh lesion responsible for the production of the pain have permitted a closer insight into the pathogenesis of causalgia.

The dramatic relief of pain produced by the injection of procaine into the region of the sympathetic ganglia suggests that the nerve elements responsible for the perception of the pain are being anesthetized. The patients will frequently state that the extremity feels numb immediately after the block and yet neurologic examination fails to reveal any additional loss of sensation other than that due to the initial nerve injury. In fact the extent of the hypoaesthesia

may actually be decreased. It is as though the center were being bombarded by a multitude of pain impulses. Sudden cutting off of a large number of these stimuli leaves the part temporarily numb. Although clinical observations have strongly indicated the "sympathetic" origin of causalgia, as Leriche⁵ was the first to point out, carefully controlled laboratory experiments in animals generally have failed to provide evidence for the transmission of afferent stimuli through the sympathetic ganglia. Only the observations of Kuntz and his associates^{6, 7} have demonstrated such pathways. Livingston¹⁰ has recently reviewed the experimental evidence and has concluded that "it is not reasonable to ascribe the benefit conferred by sympathectomy in the causalgic states to an interruption of pain pathways."

A recent concept which is more in keeping with the clinical findings is that supported by Doupe, Cullen and Chance.¹¹ They adhere to the sympathetic origin of the pain of causalgia but attribute the stimuli to impulses coming down the efferent sympathetic fibers in the mixed nerves. At the artificial synapse produced in the area of injury,¹¹ these efferent impulses are believed to spread to the sensory afferent nerves and are then carried over the dorsal roots to be perceived as pain originating in the distribution of the injured nerve. This explanation does not explain the diffuse character of the pain of causalgia nor its peculiar burning quality. However, they present considerable evidence to support this concept. In one patient with causalgia of the foot, low spinal anesthesia sufficient to block the sensory roots to the part but not high enough to affect the efferent sympathetic fibers as shown by the failure of the skin temperature to rise was sufficient to abolish the pain. This experiment was cited as evidence that all pain sensations were ultimately transmitted by way of the dorsal roots supplying the segment. On the other hand it is well recognized that the pain of causalgia may persist in spite of extensive rhizotomy. The following case is cited to raise again the question, 'Is the sensation of pain from the extremities in man carried by somatic nerves alone?'

CASE 2 (16149) — A Chinese sergeant, was wounded in the left foot on July 25, 1944. For the following six months he was treated in a hospital in the forward area for severe pain in the fore part of the foot. The pain was temporarily relieved on two occasions by paravertebral injection of procaine into the region of the lumbar sympathetic ganglia. Because of the persistence of the pain, a cordotomy was performed at the level of the second thoracic vertebra without affecting the pain and tenderness. Upon admission to the general hospital neurologic examination revealed loss of sense of pain and temperature on the left side below the fourth thoracic vertebra and complete sensory loss in the left foot except that pain and tenderness on pressure persisted in the distal end of the foot. Injection of procaine into the region of the left lumbar sympathetic ganglia caused prompt disappearance of the pain and tenderness. Determinations of the skin temperature during and after the injection showed that there was no rise. This absence of rise in skin temperature was presumably due to the interruption of all efferent vasoconstrictor impulses by the previous crushing of the peripheral nerves. Perivascular sympathectomy was then performed on the femoral artery in the groin with almost complete relief of symptoms. Ten days later, since there was still slight recurrence

of pain on pressure, a second lumbar injection was given. The pain was again completely abolished and accordingly a lumbar ganglionectomy of the first to fourth lumbar vertebra was performed. No further improvement occurred.

It may have been that, in this case, the initiating factor for pain had "escaped into the higher centers" as Livingston¹⁰ has suggested. On the other hand, the persistence of tenderness indicates more likely that there is some additional pathway which has not been interrupted.

This case is noteworthy for the fact that abolition of efferent vasoconstrictor impulses by crushing the peripheral nerves did not abolish the pain. In spite of the absence of tonic sympathetic impulses, demonstrable by no rise in skin temperature after lumbar block, the pain persisted and was relieved only by the injection of procaine into the region of the lumbar sympathetic ganglia. The partial relief afforded by periarterial sympathectomy suggests that the periarterial nerves may be in part a route for the transmission of the painful impulses. Pearse¹⁶ has cited a case of causalgia which was not relieved by lumbar sympathectomy but at a subsequent time was relieved by periarterial sympathectomy of the femoral artery. Pereira⁵ recently showed in man that pain from stimulation of the perivascular tissues is transmitted through the sympathetic ganglia. The improvement noted in the results obtained in the present series of cases when periarterial sympathectomy was added to the upper thoracic ganglionectomy is additional evidence of the significance of this pathway in the mediation of the painful impulses. Further evidence against the concept that efferent sympathetic discharges are responsible for the pain is afforded by the experience reported by Mayfield and Devine.⁴ In the treatment of causalgia of the lower extremity by lumbar sympathectomy they observed that one case was not relieved by resection of the third and fourth lumbar ganglia. However, when at a second operation the first and second ganglia were also removed the pain was relieved.

Inspection of the wounds within ten days after injury has revealed that the damaged nerves are in contact with devitalized tissue and are adherent to surrounding structures by means of plastic exudate. It is readily understandable that any slight contraction of the muscles would produce stimulation of these sensitive exposed structures. To account for the persistence of the pain it is suggested that any stimulation which produces involuntary contraction of the striated muscle in the neighborhood of the injured nerve will produce pain. The pain impulses may be carried over the sensory fibers in the sympathetic system described by Kuntz and his associates.⁶ The pathways may be both in the mixed nerves and in the periarterial network. The afferent stimuli upon entering the cord may excite contraction of the muscles which supply the region of the injury and thus occasion further stimulation of the sensitive injured structures. Paravertebral injection of procaine by abolishing the painful stimulation may break up this vicious circle. If there is extensive partial injury to the nerve, recurrence of the vicious circle generally takes place spontaneously. With a mild injury, one injection alone may afford permanent relief. In the severe cases the vicious circle can be prevented by shielding the area of injury through

accurate approximation of the exposed nerve ends. If this is impossible complete severance of all pathways is necessary in order to abolish the reflex permanently.

Nothing more than a suggestion is possible as to the mechanism of causalgia. The hypothesis of the "sympathetic" origin of the pain in man is in accord with clinical experience. This hypothesis is not in accord with the majority of observations made on experimental animals. The therapeutic implications however, are clear. It is essential to relieve the pain early before the onset of soft tissue changes. Recognizing the fact that the initial lesion is trauma to a nerve, generally incomplete severance of one of the large nerves of the extremities, prompt exploration with adequate debridement and early closure of the wound are indicated. Persistence of pain can generally be abolished by one or more injections of procaine into the region of the sympathetic ganglia. Although radical sympathetic ganglionectomy, possibly combined with periarterial sympathectomy will give relief from pain it should be used only in the event that local repair of the nerve is impossible because of complicating factors or that the pain persists in spite of repeated paravertebral injection. Sympathectomy should be performed as soon as it becomes apparent that treatment of the local lesion will not afford relief from pain.

SUMMARY

The diagnosis of causalgia was made on the basis of the relief of pain by paravertebral injection of procaine in 114 Chinese casualties selected from 2167 cases of gunshot wounds of the extremities. The causalgia was severe in twenty of these cases.

Permanent relief of pain following sympathetic block by paravertebral injection of procaine even when repeated was obtained only in the mild cases.

Partial recurrence of pain was noted in four out of six cases following preganglionic sympathectomy or ganglionectomy.

Ganglionectomy combined with periarterial sympathectomy of the subclavian artery gave complete relief of pain in seven cases of moderately severe and severe causalgia of the upper extremity. In the long standing cases of causalgia even though the pain was relieved the functional results were poor due to the secondary fibrotic changes in the soft tissues of the hand.

Early radical sympathectomy in ten cases prevented the development of contractures and other secondary changes.

Early reparative surgery within three weeks of the initial injury followed by one or two paravertebral injections of procaine was used in four cases. Relief of pain was achieved and secondary contractures were prevented.

Early relief of pain is essential in order to prevent the development of soft tissue changes. This relief can best be obtained by early reparative surgery followed when necessary by paravertebral injections of procaine.

Radical sympathectomy should be reserved for those patients in whom it is impossible to obtain clean healing of the wounds which involve the nerves or in whom the pain persists. Sympathectomy should be performed early before the development of fibrosis and contractures.

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VARIATIONS IN THE SYNDROME OF THE RUPTURED INTERVERTEBRAL DISC IN THE LUMBAR REGION

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THE syndrome of simple rupture or protrusion of the intervertebral disc has been defined very clearly in recent years, providing much clarification of the problem of low back pain. The syndrome has been recognized with increasing frequency, particularly since Mixter's publications, and today it is of major neurosurgical consideration. Approximately 80 per cent of ruptured lumbar discs elicit a classical picture, but the remaining 20 per cent present puzzling and complex variations which demand the most detailed and careful study for differential diagnosis. The site of rupture (whether lateral or transverse in relation to the spinal canal), the direction of the protrusion of the disc, and other sequelae determine the resulting symptoms and signs. The present paper is concerned with a discussion of the variations in the syndrome in relation to the anatomic changes with which they are associated.

Simple rupture or protrusion of the disc to impinge on a single spinal nerve root, as shown in Fig. 1, A, results in symptoms and signs which are relatively few and uniform. The classical picture associated with this condition may be described as follows. The subjective changes presented by patients with laterally protruding ruptured discs, as well as the objective ones found on examination, are fairly characteristic and vary mostly in intensity according to the stage of advancement. A history of trauma, single or repeated, can be obtained from the majority of these patients; the remainder of the individuals, with a few exceptions, have had a sudden onset of pain even if no history of trauma is obtainable. The pain is confined to the lumbosacral region for a variable length of time or until the protrusion of the disc takes place and the root compression is established, which results in complaints of radiating pain in the posterior aspect of one of the lower limbs. These radicular pains are variable in extent but are always influenced by motion in the lumbosacral spine and by changes in the intraspinal pressure resulting from the variability of congestion in the radicular veins brought on by increased abdominal and thoracic pressure, as during coughing, sneezing, and straining. The radicular pain at times may have localizing value, but this depends largely upon the patient's ability to observe the distribution of the radiation.

Radicular pain is frequently accompanied by paresthesia which are confined at times within the limits of the distribution of pain but more often within an area distal to that inside the range of pain. Other patients complain of mere numbness which also is felt beyond the painful area. Thus it is rather common for patients to complain of excruciating pain in the posterior

atrophy of certain muscle groups sensory impairment in certain dermatomes and finally changes in the tendon reflexes of the lower limbs

On the basis of these findings a ruptured intervertebral disc at the fourth lumbar interspace can be recognized easily when it protrudes laterally. The mechanical defensive signs are present the patient complains of sciatic pain and numbness of the leg toe and the examiner finds weakness of the anterior tibial and peroneal muscle groups decreased knee jerk and sensory impairment over the anterior aspect of the leg and dorsum of the foot. Likewise, rupture at the fifth lumbar interspace and compression of the first sacral root can be diagnosed when the patient complains of numbness in the two lateral toes along with sciatic pain and when examination reveals drooping of the gluteal fold decrease or absence of ankle jerk, and impairment of sensation over the lateral aspect of the leg and foot.

In contrast with this clearly defined clinical syndrome are the variations in the symptoms and signs associated with other types of rupture of the intervertebral discs or complications and progressive changes in the simple type. Correlation of clinical with operative findings has revealed a number of conditions responsible for variations in the syndrome these are

- 1 The rupture has taken place higher than the fourth lumbar interspace
- 2 Lateral protrusion has not occurred or the protrusion is large enough to affect more than one or two nerve roots
- 3 The protrusion has been bilateral
- 4 Two or more adjacent discs have ruptured
 - 1 The main bulk of the ruptured disc is no longer attached to its interspace but has wandered into the spinal canal
- 6 The protrusion is so massive that it completely blocks the spinal canal and thus produces the syndrome of cauda equina

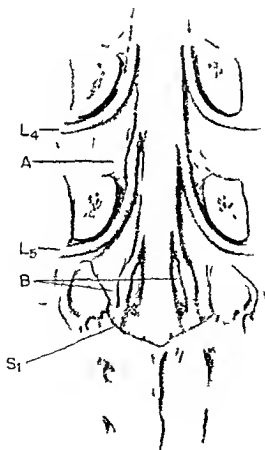
First ruptures at the higher interspaces cause complaints mostly of back pain or flank pain and the helpful sciatic distribution is missing as are many of the other easily detected signs of rupture of the lower discs. The following case history briefly summarized may serve as an illustration.

CASE 1 (History No 7647) A 39 year old man experienced onset of pain in the right lumbar region ten weeks before admission. There was no radicular pain but pain aggravated by motion in lumbosacral spine and by increased intraspinal pressure. Abnormal objective findings were paravertebral muscle spasm in right lumbosacral region with tenderness on pressure in this area. In this case there was no scoliosis no limitation of forward bending no limitation of straight leg raising no tenderness of sciatic nerves no motor weakness and no sensory impairment. Lasegue's sign was negative bilaterally. Tendon reflexes were active and equal in the lower limbs. Fluoroscopy was carried out after intraspinal injection of lipiodol and a large filling defect was encountered at the first lumbar interspace on the right side. Operation revealed a ruptured disc in this space seen intradurally as a protrusion occupying the right half of the spinal canal and displacing the cauda equina posteriorly.

Second when the ruptured disc fails to protrude laterally (Fig 2) or if it is sufficiently large (Fig 3) it may compress several roots and may even affect all of the roots that have not left the spinal canal by their respective interver-

thigh and calf and simultaneously of numbness in the big toe or the little and fourth toes. Few will feel pain down to the toes, though such a complaint is encountered occasionally.

The objective changes found after protrusion of the disc may be classified as follows: (1) changes characteristic of a ruptured lumbar disc and (2) changes that have localizing value with respect to the particular nerve roots compressed. The former changes are mechanical and defensive and are due to bodily responses induced to guard against the shocking pain, for example the paravertebral muscle spasm, abnormal posture of the spine, limitation of straight leg raising, presence of Lasegue's sign. The localizing changes are neuropathologic in nature and therefore of much graver significance. Such changes are briefly: the early selective weakness and hypotonia followed by



atrophy of certain muscle groups sensory impairment in certain dermatomes and finally, changes in the tendon reflexes of the lower limbs

On the basis of these findings a ruptured intervertebral disc at the fourth lumbar interspace can be recognized easily when it protrudes laterally. The mechanical defensive signs are present, the patient complains of sciatic pain and numbness of the big toe, and the examiner finds weakness of the anterior tibial and peroneal muscle groups, decreased knee jerk and sensory impairment over the anterior aspect of the leg and dorsum of the foot. Likewise, rupture at the fifth lumbar interspace and compression of the first sacral root can be diagnosed when the patient complains of numbness in the two lateral toes along with sciatic pain and when examination reveals drooping of the gluteal fold, decrease or absence of ankle jerk, and impairment of sensation over the lateral aspect of the leg and foot.

In contrast with this clearly defined clinical syndrome are the variations in the symptoms and signs associated with other types of rupture of the intervertebral discs or complications and progressive changes in the simple type. Correlation of clinical with operative findings has revealed a number of conditions responsible for variations in the syndrome. These are:

- 1 The rupture has taken place higher than the fourth lumbar interspace
- 2 Lateral protrusion has not occurred or the protrusion is large enough to affect more than one or two nerve roots
- 3 The protrusion has been bilateral
- 4 Two or more adjacent discs have ruptured
- 5 The main bulk of the ruptured disc is no longer attached to its interspace but has wandered into the spinal canal
- 6 The protrusion is so massive that it completely blocks the spinal canal and thus produces the syndrome of cauda equina.

First ruptures at the higher interspaces cause complaints mostly of back pain or flank pain and the helpful sciatic distribution is missing as are many of the other easily detected signs of rupture of the lower discs. The following case history, briefly summarized, may serve as an illustration.

CASE 1 (History No. 76477) —A 39-year-old man experienced onset of pain in the right lumbar region ten weeks before admission. There was no radicular pain but pain aggravated by motion in lumbosacral spine and by increased intraspinal pressure. Abnormal objective findings were paravertebral muscle spasm in right lumbosacral region with tenderness on pressure in this area. In this case there was no scoliosis, no limitation of forward bending, no limitation of straight leg raising, no tenderness of sciatic nerves, no motor weakness and no sensory impairment. Lasègue's sign was negative bilaterally. Tendon reflexes were active and equal in the lower limbs. Fluoroscopy was carried out after intraspinal injection of lipiodol and a large filling defect was encountered at the first lumbar interspace on the right side. Operation revealed a ruptured disc in this space, seen intradurally as a protrusion occupying the right half of the spinal canal and displacing the cauda equina posteriorly.

Second, when the ruptured disc fails to protrude laterally (Fig. 2) or if it is sufficiently large (Fig. 3) it may compress several roots and may even affect all of the roots that have not left the spinal canal by their respective interver-

tebral foramina. This syndrome may begin with inconspicuous complaints of low back pain that may suddenly progress into the well-established picture of a cauda equina tumor or it may acquire the character of a single root compression for a variable length of time and it may become bilateral in character.

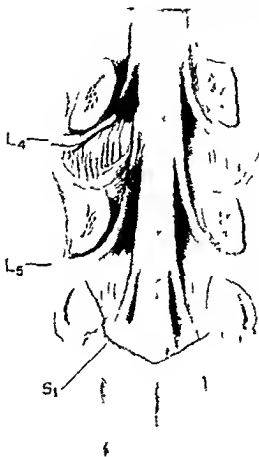


Fig. 2.—Lateral view of the spine at the fourth lumbar interspace with compression of the adjacent fifth lumbar and first sacral root.

The complaint of a patient so affected will naturally differ from those caused by a steady solid unilateral compression and it is particularly the changeability of symptoms that is important here. In such cases the complaints are often unsystematic and the defensive mechanical signs are quite different, not being nearly so outspoken. The neuropathologic signs are often vague and late in developing according to the extent of compression in the one case and the number of roots affected in the other. Only the subjective symptoms may be manifest for a long time before the compression reaches a

degree such as to produce objective changes. The following cases will serve as illustrations.

CASE 2 (History No. A94792)—A 47-year-old man experienced gradual onset of low back pain three years prior to admission. Severe exacerbation of low back pain associated with bilateral hip pain radiating down the posterior thighs to the knees was present during a few months prior to admission. Abnormal objective findings were diminished lordosis and an almost complete rigidity of the lumbar spine, forward bending limited to 45 degrees, marked bilateral paravertebral lumbar muscle spasm, tenderness to palpation in the lumbosacral area, straight leg raising limited to 45 degrees bilaterally, and Las'gue's sign positive bilaterally. In this case there was no tenderness of the sciatic nerves, no muscle weakness, and no sensory impairment. Tendon reflexes in the lower limbs were knee jerks ++ right, +++ left, ankle jerks + right ++ left. Fluoroscopy carried out after intraspinal injection

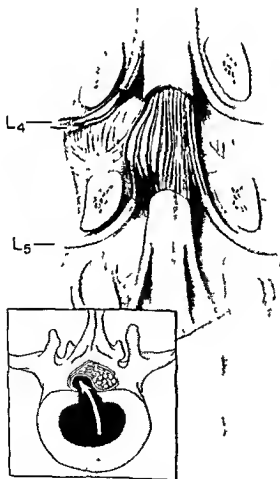


Fig. 3—Large medial protrusion at the fourth lumbar interspace with multiple root compression.

of lipiodol, showed a large filling defect at the fourth lumbar interspace. Operation revealed a ruptured disc at this level, the protrusion extending across the entire space, primarily on the right side. The protrusion was also displaced upward over the body of the fourth lumbar vertebra.

CASE 3 (History No. B42091)—A 45 year old man had gradual onset of low back pain two years before admission. There was radiation of pain to the left hip and down the posterior left thigh ten months before admission. Five months later severe exacerbation of low back pain with radiation to both posterior thighs, more marked on the left side, was present, with range down to the calf and associated with numb feeling in both feet. There were no bladder or bowel disturbances. Pain increased by motion in the lumbosacral spine and on increased intraspinal pressure. Abnormal objective findings were moderate tenderness on palpation of lumbosacral area, forward bending limited to 45 degrees by low back and bilateral hip pain. In this case there was no scoliosis, no paravertebral muscle spasm, straight leg raising unlimited bilaterally, Lasegue's sign negative bilaterally, no motor weakness, and no sensory impairment. Tendon reflexes in the lower limbs showed minimally decreased left knee jerk, the ankle jerks were active and equal. Fluoroscopy after intraspinal injection of lipiodol showed an almost complete block at the third lumbar interspace. Operation revealed a ruptured disc at this level, protruding 1 cm. backward into the spinal canal.

A third variation of the rupture (Fig. 1B) is the bilaterally protruding disc, in which condition bilateral sciatica is the main complaint and the usual signs of a single root compression are present on both sides. However, the difference between the second variety and this one is frequently slight and fleeting, at times a matter only of degree. The following case may illustrate this.

CASE 4 (History No. B4413)—A 29 year old woman experienced sudden onset of severe pain in the right hip without any obvious cause thirteen months prior to admission, she was in the eighth month of pregnancy. Right sciatic pain soon developed ranging down to the heel, together with low back pain. Six weeks prior to admission severe exacerbation of low back pain associated with bilateral sciatic pain and numbness in both feet was present. Abnormal objective findings were marked tenderness on palpation over lumbosacral area, lumbosacral scoliosis with convexity to the left, marked tenderness of both sciatic nerves and moderate, nonselective weakness of the lower limbs, more marked on the right side. Straight leg raising was limited to 45 degrees bilaterally and there was sensory impairment over the lateral aspect of the leg and foot from the knee down bilaterally. Tendon reflexes in the lower limbs were knee jerks ++ bilaterally, ankle jerks 0 right + left. Operation revealed a ruptured disc at the fifth lumbar interspace protruding laterally on both sides, with complete rupture on the right side.

The fourth variation which may render the diagnosis difficult and in some respects even mislead in the detection of a ruptured intervertebral lumbar disc in the usual conception of that syndrome is seen when multiple ruptures (Fig. 1, A and B) have occurred and the protrusions necessarily compress more than one nerve root. The multiple ruptures may be either unilateral or bilateral. It is to be noted that one disc protruding laterally may impinge at times on two adjacent roots. This however does not cause much confusion as the signs from one of the roots usually predominate over those from the other root under compression. The following case illustrates clearly how extensive the lesion may be and therefore, how complicated are the resulting signs.

CASE 5 (History No. 22719)—A 59 year old white man had a history of repeated attacks of low back pain of twenty five years' duration. He had had attacks of sciatica on the left side during a period of seven years. The pain in the present attack of sciatica originated in the left hip and radiated down the anterior aspect of the thigh to one knee. Pain was aggravated by increased intraspinal pressure and motion in lumbosacral spine. Abnormal objective findings were marked tenderness on palpation in the lumbosacral area, straight leg raising unlimited on right side and 45 degrees on left, and Lasègue's sign positive on left. There was marked atrophy of the left anterior tibial and peroneal muscle groups, hypotonia of all muscle groups, and marked generalized weakness of the entire left lower limb, with an almost complete foot drop. There was sensory impairment over the anterior aspect of the left thigh and leg down to ankle. The knee jerks were absent bilaterally, ankle jerks were + on right, 0 on left. In this case there was no scoliosis, no paravertebral spasm, but moderate stiffness of the lumbar spine. After intraspinal injection of lipiodol, fluoroscopy showed irregular defects at the second, third, and fourth lumbar interspaces. Operation revealed an extremely large transversely protruding disc obliterating completely the subarachnoid space at the second lumbar interspace, a laterally protruding disc at the third lumbar interspace on the right side, and a laterally protruding ruptured disc at the fourth lumbar interspace on the left side.

A fifth variety arises when a large portion of the ruptured disc becomes detached and escapes from its interspace, as seen in Fig. 4. These discs may wander and settle somewhere within the spinal canal or in the extradural space, and they have been found even posterior to the cauda equina. Naturally, the complaints and signs will change from time to time in such a case, as this syndrome usually will begin as that of an ordinary lateral protrusion and then later deviate from the pattern when the disc wanders and more than one root becomes involved. The following short case history may show this grossly

CASE 6 (History No. B77241)—A 41 year old man, in 1926, experienced sudden onset of severe pain in the low back, radiating into the calf of the right leg. A body cast was applied and worn for twenty three weeks during which period the pain slowly diminished and finally disappeared. The patient was asymptomatic then until 1940, when the right sciatic pain re-
 occurred after heavy lifting, this time associated with weakness of the right foot. Pain disappeared in one week and the weakness of the right foot diminished gradually. In December, 1945, or one month prior to admission, the patient again strained his back and experienced an immediate onset of pain in that region, this time radiating into the left calf and occasionally into the right. One week later foot drop on the left was observed. Pain was aggravated by increased intraspinal pressure and motion in the lumbosacral spine. After admission, the sciatic pain on the left side disappeared but reappeared and became confined to the right side. Positive pathologic findings were lumbosacral scoliosis, convex over to the right, bilateral paravertebral lumbar muscle spasm, forward bending limited to 15 degrees, tenderness on palpation over the lumbosacral area, tenderness of the right sciatic nerve, straight leg raising 75 degrees on the left, 65 on the right; Lasègue's sign negative bilaterally, complete foot drop on the left, marked weakness of dorsiflexion of the foot on the right, and sensory impairment over the lateral aspect of both legs and feet below the knee. Reflexes were knee jerks ++ right, + left, ankle jerks 0 right ± left. At operation, this patient was found to have a markedly narrowed fourth lumbar interspace. The disc had ruptured through the posterior longitudinal ligament and was lying free as a loose fragment in the extradural space over the posterior lateral surface of the dura, and another fragment was present lateral to the nerve root and dura.

Sixth, when the protrusion is exceptionally large, extending across the entire space (Fig. 5), most commonly encountered at the fourth and fifth lumbar

of lipiodol showed a large filling defect at the fourth lumbar interspace. Operation revealed a ruptured disc at this level the protrusion extending across the entire space, primarily on the right side. The protrusion was also displaced upward over the body of the fourth lumbar vertebra.

CASE 3 (History No. B4,091)—A 45 year old man had gradual onset of low back pain two years before admission. There was radiation of pain to the left hip and down the posterior left thigh ten months before admission. Five months later severe exacerbation of low back pain with radiation to both posterior thighs, more marked on the left side was present, with range down to the calf and associated with numb feeling in both feet. There were no bladder or bowel disturbances. Pain increased by motion in the lumbosacral spine and on increased intraspinal pressure. Abnormal objective findings were moderate tenderness on palpation of lumbosacral area, forward bending limited to 45 degrees by low back and bilateral hip pain. In this case there was no scoliosis, no paravertebral muscle spasm, straight leg raising unlimited bilaterally, Lasegue's sign negative bilaterally, no motor weakness, and no sensory impairment. Tendon reflexes in the lower limbs showed minimally decreased left knee jerk, the ankle jerks were active and equal. Fluoroscope after intraspinal injection of lipiodol showed an almost complete block at the third lumbar interspace. Operation revealed a ruptured disc at this level protruding 1 cm. backward into the spinal canal.

A third variation of the rupture (Fig 1B) is the bilaterally protruding disc, in which condition bilateral sciatica is the main complaint and the usual signs of a single root compression are present on both sides. However, the difference between the second variety and this one is frequently slight and fleeting at times a matter only of degree. The following case may illustrate this.

CASE 4 (History No. B23163)—A 39 year old woman experienced sudden onset of severe pain in the right hip without any obvious cause thirteen months prior to admission. She was in the eighth month of pregnancy. Right sciatic pain soon developed ranging down to the heel together with low back pain. Six weeks prior to admission severe exacerbation of low back pain associated with bilateral sciatic pain and numbness in both feet was present. Abnormal objective findings were marked tenderness on palpation over lumbosacral area, lumbodorsal scoliosis with convexity to the left, marked tenderness of both sciatic nerves and moderate, nonselective weakness of the lower limbs more marked on the right side. Straight leg raising was limited to 45 degrees bilaterally and there was sensory impairment over the lateral aspect of the leg and foot from the knee down bilaterally. Tendon reflexes in the lower limbs were knee jerks ++ bilaterally, ankle jerks 0 right + left. Operation revealed a ruptured disc at the fifth lumbar interspace protruding laterally on both sides with complete rupture on the right side.

The fourth variation which may render the diagnosis difficult and in some respects even mislead in the detection of a ruptured intervertebral lumbar disc in the usual conception of that syndrome is seen when multiple ruptures (Fig 1, A and B) have occurred and the protrusions necessarily compress more than one nerve root. The multiple ruptures may be either unilateral or bilateral. It is to be noted that one disc protruding laterally may impinge at times on two adjacent roots. This however, does not cause much confusion as the signs from one of the roots usually predominate over those from the other root under compression. The following case illustrates clearly how extensive the lesion may be and therefore how complicated are the resulting signs.

CASE 7 (History No B40164)—A 66 year old man had sudden onset of low back pain and left sciatic pain nine months prior to admission. At the same time there was moderate pain in the posterior aspect of the right lower limb coming on after heavy lifting. A few days later there were urinary incontinence weakness in both lower limbs and marked constipation. The patient was confined to bed for nine months during which time there was complete impotence and incontinence. All muscle findings were patient unable to stand without crutches marked tenderness on palpation of lumbosacral area both sciatic nerves tender straight leg raising limited to 0 degrees on left and 30 on right and Lasague's sign positive bilaterally. There were marked weakness and atrophy of both the dorsiflexors and the plantar flexors bilaterally more marked on the left side. Both gluteal folds were atrophic and toneless. Sensory examination revealed a saddle anesthesia extending down the posterior thighs and leg on both sides including the lateral aspect of feet and the fourth and fifth toes. Tendon reflexes were knee jerks +++ right +++ left ankle jerks absent bilaterally.

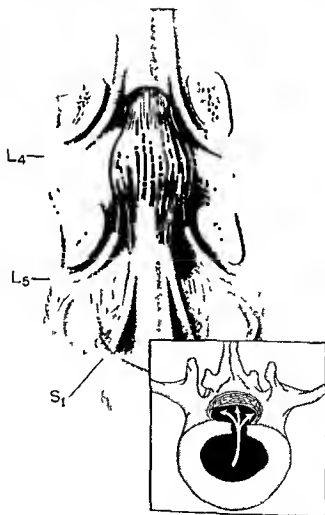


Fig. 5—Massive transverse protrusion at the fourth lumbar interspace with compression of the entire cauda equina.

interspaces it produces a more or less complete block of the spinal canal and thus compression of the entire cauda equina. The picture simulates that of a cauda equina tumor, that is the bladder and bowel disturbances along with sexual impotency predominate in the presence of saddle anesthesia and weakness of the lower limbs. The history in these cases is particularly important

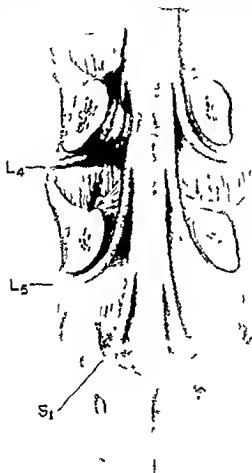


FIG. 4.—Wandering line. Rupture occurred at the fourth lumbar interspace where the tear is seen, and the displaced disc fragment is seen over the posterior surface of the body of the fourth lumbar vertebra compressing the fourth lumbar root.

because if there is a background of trauma or if the history reveals a sudden onset of pain and sudden development of the neuropathologic signs the assumption is well justified that a ruptured disc and not a tumor is responsible for the disability. If this is recognized early the chances of recovery are so much the greater.

at the fourth or fifth lumbar interspace, exploration of both interspaces is the rule. In such cases continued complaint of pain is considered an indication for myelography in order to avoid missing multiple discs.

The massive protrusions that obliterate the spinal canal exert pressure on all roots that have not left the canal. These are encountered most frequently at the fourth and fifth lumbar interspaces. These conditions are associated with the three most discouraging signs of nervous diseases, namely, loss of urinary and fecal control along with sexual impotency. Unfortunately these signs are frequently accompanied by incurable conditions. A careful consideration of the history, however, will simplify differentiation, since it is well known now that a ruptured disc often is responsible for paraparesis associated with urinary and fecal incontinence and loss of sexual potency. Whether these neuropathologic signs are reversible or not depends upon their duration.

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plantar reflexes down. Fluoroscopic, after intra-axial injection of lipiodol revealed a large defect in the lipiodol shadow overlying the fourth and fifth interspaces. Operation disclosed a ruptured disc at the fifth lumbar interspace, with the largest protrusion in the midline but extending out to both sides. The disc at the fourth interspace also was ruptured and protruded laterally toward the right side.

COMMENT AND CONCLUSION

The observations described in the present paper reveal a number of variations that occur in the rupture of the intervertebral disc and in the resulting associated syndromes. While much interest has been shown in differential diagnosis of the simple ruptured disc, less attention has been given to the detection and recognition of the more complicated or progressive types of the condition. From a consideration of the differences in the pathologic anatomy of the various types it is obvious that considerable differences should be seen in the corresponding signs and symptoms. A basis for differential diagnosis of the more complex ruptures from other neurologic conditions can be established chiefly by careful correlation of the clinical findings with those encountered at operation.

At the onset, the histories of the individual varieties may not differ greatly. Low back pain is the outstanding complaint in all cases. Sciatic pain may be felt on one or both sides or not at all. Theoretically, it should be possible clinically to detect a simple ruptured protruding disc at the higher lumbar interspaces, but many other ailments induce the symptoms and findings of patients thus affected. A symptom of much value in indicating rupture of the disc in this situation is the complaint of radicular pain.

The protrusion that occurs otherwise than laterally or which is large enough will always affect several roots and therefore, widen the sphere of possible rupture and compression to that of more than one interspace. Confusion may arise in differentiating this condition from that in which one laterally protruding disc compresses two adjacent nerve roots; for example the disc at the fifth lumbar interspace may impinge upon both the fifth lumbar and the first sacral roots simultaneously. Such a protrusion however will cause a fairly clear picture of sciatica usually with predominance of signs from one of the two roots. In the presence of such signs and symptoms both spaces should be explored routinely in order to avoid overlooking one of two discs which naturally could and often do produce a similar syndrome.

In the instances of certain of the types definite diagnosis can be reached only with the aid of myelography. Difficulties are encountered in the diagnosis of multiple ruptures—for example the lateral protrusion at three interspaces on one or both sides as illustrated in Case 5. Diagnosis of ruptures higher than the fourth interspace and those which fail to protrude laterally is likewise greatly facilitated by myelography. Use of myelography is of especial value in the location of the wandering disc in order to avoid unnecessary exploration of several interspaces at operation. It should be emphasized that myelography is not indicated in all cases but only in those in which clinical localization of the rupture is not possible. In all apparently clear cases of lateral protrusions

terminal portion of the loop excluded. If the blood supply is dubious the clamp should be left on for five to ten minutes as the circulation frequently improves during this period. The presence or absence of pulsation in the smaller mesenteric vessels and the color and peristaltic activity of the intestine are the criteria to be followed in testing the adequacy of the circulation. If a sufficient length of jejunum with adequate circulation is obtained in this manner obviously no further procedures are necessary other than care to prevent obstruc-

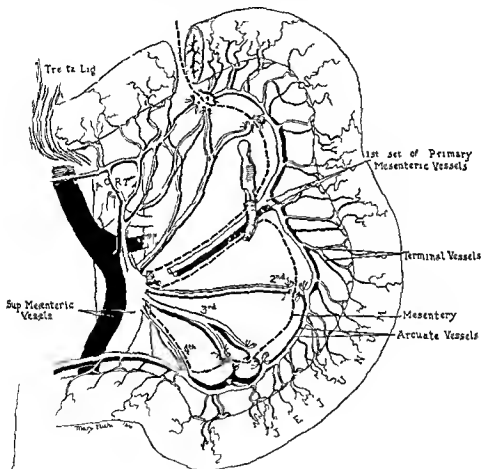


Fig 1—Division of jejunum and mesenteric vessels with bulldog clamp occluding first set of primary mesenteric vessels. arcuate vessels unobstructed throughout length of jejunal loop

tion of the vessels by twisting when the jejunum is placed over the costal margin and beneath the skin of the chest wall. If, however, the arteries and veins to be divided are large well developed vessels the vessels distal to this point are usually smaller and are inadequate to provide the circulation for the mobilized loop. It is this type of vascular arrangement in which anastomosis of the mesenteric and mammary blood vessels is indicated.

A MODIFICATION OF THE ROUX TECHNIQUE FOR ANTHORACIC ESOPHAGEAL RECONSTRUCTION

ANASTOMOSIS OF THE MESENTERIC AND INTERNAL MAMMARY BLOOD VESSELS

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ONE of the most satisfactory methods of esophageal reconstruction thus far developed is that originally described by Roux¹ in 1907. In this method the intestine is divided a short distance from the ligament of Treitz and a long segment of jejunum is mobilized by severing the first three or four primary mesenteric vessels, the circulation of the mobilized loop being maintained through the arcuate vessels which run parallel with the intestine. The mobilized loop of jejunum is placed beneath the skin of the anterior chest wall, the upper end is anastomosed to the proximal esophagus and the continuity of the intestinal tract is restored in the abdomen by an end to side anastomosis distal to the mobilized loop. Lindin² reported eleven successful cases completed by this method. He stressed, however, the importance of the variations of the vascular pattern in the jejunal mesentery and stated that at times the size or arrangement of the vessels may be such as to preclude the performance of this type of reconstruction. Oelsner and Owens reviewed the literature up to 1934 and found that gangrene of the jejunal loop developed in 22 per cent of the reported cases.

This paper reports a method of anastomosing one of the primary vessels in the mesentery of the mobilized loop to the internal mammary vessels thereby reducing the hazard of necrosis of the jejunal loop due to insufficient circulation and overcoming some of the difficulties encountered in cases with an unfavorable mesenteric vascular pattern. The size of the vessels to be anastomosed makes the procedure unsuitable for infants or small children.

TECHNIQUE

The abdomen is entered through a left upper rectus or midline incision and the first portion of the jejunum is identified at a point 8 to 10 cm. from the ligament of Treitz. The intestine and the arcuate vessels are divided. The size and position of the first five primary mesenteric vessels are inspected. To free sufficient jejunum to reach above the clavicle it is usually necessary to divide four of the primary mesenteric vessels. Although this detail must be determined for each case (Fig. 1). Two primary mesenteric arteries and veins can be divided with impunity. Before the third and fourth sets are divided however they should be occluded with a bulldog clamp and the circulation of the

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*The editor of the journal in which his paper appeared credited him with twenty-one completed cases by this method at the time of publication.

ligated at the lower angle of the incision, and the upper ends are clamped with bulldog clamps. An end to end anastomosis is performed between the arteries and veins with a continuous 00000 silk suture (Fig 2). A Beebe binocular loupe magnifying lens aids in this portion of the procedure. After the anastomosis is completed it is possible to divide additional mesenteric vessels if greater length of the loop is needed. A subcutaneous channel is made over the anterior chest wall and the end of the intestinal loop is brought to the outside through the skin of the neck along the anterior border of the left sternomastoid muscle. The continuity of the intestinal tract is restored by an end to side anastomosis between the proximal end of the jejunum and the side of the jejunum distal to the mobilized loop. At a subsequent operation the cervical esophagus is mobilized as previously described,⁴ and at the third operation the esophagojejunal anastomosis is completed.

CASE REPORT

W. C., a 28 year old colored man, was admitted to the Johns Hopkins Hospital on April 5, 1940, because he was unable to retain food or liquids.

In October, 1913, he swallowed lye and shortly thereafter a severe stricture of the esophagus developed. From January, 1944, until October, 1945, he had received weekly esophageal dilations at another hospital but had been able to swallow and retain only liquids. After the dilations were discontinued he began to vomit more frequently and this difficulty steadily increased up until the time of admission. He had lost thirty pounds and was severely dehydrated. X-ray examination of the esophagus and esophagoscopy demonstrated an impermeable benign stricture in the middle third of the esophagus.

On April 15, 1946, the first stage of an intrathoracic esophageal reconstruction was performed. Through an upper midline incision the first portion of the jejunum and the arcuate vessels were divided about 10 cm. from the ligament of Treitz. The first and third primary mesenteric arteries and veins were fairly large, and the third vessels branched about one third of the way from the root of the mesentery. The second, fourth, and fifth vessels were small and poorly developed. Distal to this region the branching of the mesenteric vessels made them unsuitable for extensive mobilization of the intestine. With the use of methods previously described an adequate length of viable jejunum could not have been mobilized, and it was decided to anastomose the first set of primary mesenteric vessels to the internal mammary vessels as described in the foregoing sections.

Immediately upon release of the bulldog clamps pulsations which had previously been absent were seen in the small terminal intestinal arteries at the end of the intestinal loop and the appearance of this portion of the loop, which had become cyanotic, returned to normal. The hyperactive peristalsis of the loop ceased and the bowel responded with normal peristaltic contractions to mechanical stimulation.

After testing with temporary occlusion, the second branch of the third primary mesenteric artery was divided without affecting the circulation in the terminal portion of the jejunal loop. This step permitted the end of intestine to be brought to the outside through an opening in the left lower cervical region. The loop entered the abdomen through the upper portion of the midline incision. The continuity of the intestinal tract was restored.

At the second operation twelve days later the cervical esophagus was mobilized and placed subcutaneously as previously described.⁴ After operation an esophageal fistula developed through this incision, either from trauma at the time of operation or as a result of pressure necrosis at the site of the "muscular sling" which held the esophagus anteriorly (Fig 3). This mishap delayed the third operation until thirty three days later.

The first or second pair of primary mesenteric vessels is clamped with bull dog clamps the proximal ends are ligated near the superior mesenteric vessels and the vessels are divided. It is then necessary to decide at what point these vessels should be anastomosed to the internal mammary vessels to allow the jejunal loop to extend to the desired level in the neck. At the selected site a longitudinal incision is made along the left border of the sternum and two costal cartilages are resected. The internal mammary vessels are exposed and

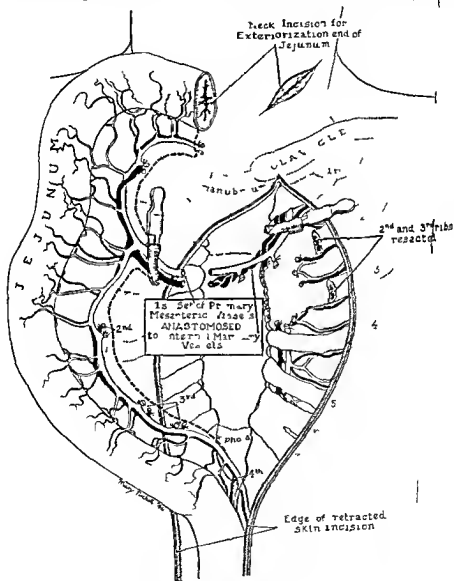


Fig. 2—Jejunal loop advanced onto thorax, second and third costal cartilages resected and internal mammary vessels prepared for anastomosis to primary mesenteric vessels.

The chief disadvantage of the method has been the frequent inability to obtain a sufficient length of viable jejunum to reach above the level of the esophageal obstruction. This difficulty is largely due to normal variations in the mesenteric vascular pattern to the proximal jejunum. Excessive fat in the mesentery may also interfere. Yudin has amply demonstrated that when the vascular arrangement is favorable a sufficient length of jejunum can be obtained to reach to the mastoid region. The percentage of cases in which an unfavorable



Fig 4.—Patient two and one half months after completion of antethoracic esophagus. Incision now all well healed and patient has gained fifteen pounds.

vascular pattern is encountered is unknown. Ochsner and Owens report to 1934 of the occurrence of gangrene in 22 per cent of the reported cases in which this method was attempted suggests that it may be high. It is in this group of patients that one of the first two sets of primary mesenteric vessels is apt to be large. The modification of the procedure suggested in this paper utilized these well developed vessels for a blood vessel anastomosis to preserve to some extent the circulation of the jejunal loop.

It had been planned to anastomose the end of the jejunal loop to the side of the esophagus but the development of the esophageal fistula which arose on the posterior surface of the esophagus necessitated division of the esophagus closure of the aboral end and performance of an end to end anastomosis between the jejunal loop and the oral end of the esophagus. This junction was made with two rows of interrupted chromic catgut sutures. The anastomosis which was at the level of the thyroid cartilage, healed uneventfully. Two weeks after operation the patient was given liquids by mouth. A few days later he was permitted to take solid foods, the first he had swallowed and retained in two and one-half years. Following this he was able to eat all varieties of foods. The passage of food through the intestinal loop was slower than normal but was unobstructed (Fig. 4).

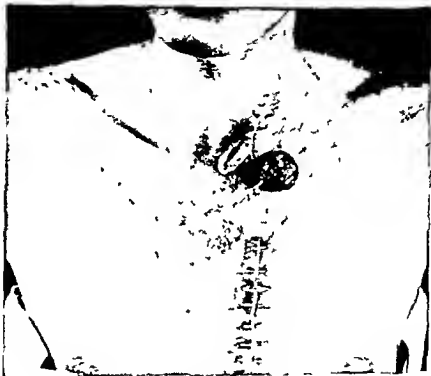


Fig. 3—Upper end of jejunal loop exteriorized above left clavicle. Neck incision for mobilization of cervical esophagus.

SUMMARY

The Roux procedure for antethoracic esophageal reconstruction has the great advantage over other methods of esophageal repair of accomplishment in two or three stages. Yudin has reported cases completed in a single operation although he recommended that the operation usually be divided into two stages. The procedure provided a tube lined with mucous membrane with a single esophageal anastomosis and an intraperitoneal end-to-side intestinal anastomosis. Except in the very high pharyngeal strictures it obviates the need for any type of skin tube and the precarious skin mucous membrane anastomosis.

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ALPUB

THE USE OF TESTOSTERONE PROPIONATE IN THE TREATMENT OF ADVANCED CARCINOMA OF THE BREAST

II THE TREATMENT OF OSSEOUS METASTASES

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IN A preliminary communication the effects of large doses of testosterone propionate on advanced carcinoma of the female breast were described. The results obtained in twelve patients who received this therapy, nine with wide spread soft part disease and three with osseous metastases, were reported at the end of six months of treatment. In the present communication we report the subsequent course of the three patients with osseous metastases described in the previous publication and present the results obtained in an additional group of eleven patients with osseous metastases from carcinoma of the breast.

A S (Case 2 in the preliminary report) developed metastatic disease of the lumbar spine and pelvis about ten years after a radical mastectomy. Testosterone therapy was instituted in April, 1945, and administered over a period of ten weeks for a total of 2,400 mg. After five weeks of therapy the patient became asymptomatic and maintained this status for five months. The osseous metastases became calcified.

Subsequent to the preliminary report she developed diplopia. Examination revealed a paralysis of the left upper eyelid and of the extraocular muscles supplied by the left third nerve. This was due to a central lesion, probably metastatic.

Testosterone therapy was reinstituted on Sept. 13, 1945. For a period of nine weeks 200 mg. of the androgen were administered twice a week for a total dose of 3,600 mg. The patient's general condition gradually deteriorated during this period. Roentgenographic studies of the lumbar spine and pelvis in November, 1945, revealed no significant changes upon comparison with previous views; that is, the metastatic areas had remained calcified. Studies of the chest in December, 1945, revealed metastases in the lung parenchyma. About one month later the patient developed a metastatic nodule on the scalp. Her last visit to the clinic was in January, 1946. She was in the terminal stage of the disease.

S K (Case 3 of the original group) had a primary inoperable carcinoma of the breast the pelvis, femora, ribs,
10 1945. Within two
um in the lesions. The
androgen was administered over a period of thirteen weeks for a total dosage of 4,100 mg.

Subsequent to the preliminary report the patient remained asymptomatic for approximately nine months. She then developed metastatic nodules in the skin of the neck and scalp. The postcervical lymph nodes became enlarged and hard. Roentgenograms made at this time revealed evidence of pulmonary metastasis and decalcification of the previously calcified osseous metastases.

Testosterone therapy was reinstituted and the patient received 250 mg. twice a week over a period of sixteen weeks. For the following four weeks she was given 200 mg. bi-weekly and 100 mg. twice a week for the subsequent fifteen weeks. The total dosage since reinstitution of the therapy was 5,250 mg. of the androgen.

The patient reported to the hospital for a period of thirteen months from the time the testosterone therapy was instituted. Roentgenograms at the end of this period disclosed

It has not been possible to demonstrate directly the patency of this blood vessel anastomosis after the conclusion of this type of operation but it is believed that if the anastomosis remains patent for a matter of four or five days the circulation of the mobilized loop will have adjusted itself through the longitudinal arcade vessels. After a period of two or three weeks collateral circulation through the subcutaneous tissue should be sufficient to maintain the intestine as was previously demonstrated by Longmire and Ravitch.⁴

CONCLUSIONS

1 The Roux type of antethoracic esophageal reconstruction is one of the most satisfactory methods of esophageal repair.

2 Unfavorable arrangement of the primary mesenteric vessels to the first portion of the jejunum may at times make it impossible to obtain a sufficient length of intestine to reach above the level of the esophageal obstruction.

3 In certain cases where the mesenteric vascular pattern is unfavorable anastomosis of one of the primary mesenteric arteries and veins to the internal mammary artery and vein will ensure an adequate blood supply to the mobilized intestine.

REFERENCES

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- 2 Yudin Laryng Surg
- 3 Olin the literature
- 4 Longmire an artificial

THE USE OF TESTOSTERONE PROPIONATE IN THE TREATMENT OF ADVANCED CARCINOMA OF THE BREAST

II THE TREATMENT OF OSSEOUS METASTASES

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IN A preliminary communication the effects of large doses of testosterone propionate on advanced carcinoma of the female breast were described. The results obtained in twelve patients who received this therapy, nine with wide spread soft part disease and three with osseous metastases, were reported at the end of six months of treatment. In the present communication we report the subsequent course of the three patients with osseous metastases described in the previous publication and present the results obtained in an additional group of eleven patients with osseous metastases from carcinoma of the breast.

A. S. (Case 2 in the preliminary report) developed metastatic disease of the lumbar spine and pelvis about ten years after a radical mastectomy. Testosterone therapy was instituted in April, 1945, and administered over a period of ten weeks for a total of 2,400 mg. After five weeks of therapy the patient became asymptomatic and maintained this status for five months. The osseous metastases became calcified.

Subsequent to the preliminary report she developed diplopia. Examination revealed a paralysis of the left upper eyelid and of the extraocular muscles supplied by the left third nerve. This was due to a central lesion, probably metastatic.

Testosterone therapy was reinstituted on Sept. 13, 1945. For a period of nine weeks 200 mg. of the androgen were administered twice a week for a total dose of 3,600 mg. The patient's general condition gradually deteriorated during this period. Roentgenographic studies of the lumbar spine and pelvis in November, 1945, revealed no significant changes upon comparison with previous views that is the metastatic areas had remained calcified. Studies of the chest in December 1945, revealed metastases in the lung parenchyma. About one month later the patient developed a metastatic nodule on the scalp. Her last visit to the clinic was in January 1946. She was in the terminal stage of the disease.

S. K. (Case 3 of the original group) had a primary inoperable carcinoma of the breast with widespread metastasis to the cervical, dorsal, and lumbar spine, the pelvis, femora, ribs, and shoulder girdles. Testosterone therapy was instituted on March 10, 1945. Within two months there was a subsidence of the pain and a deposition of calcium in the lesions. The androgen was administered over a period of thirteen weeks for a total dosage of 4,100 mg.

Subsequent to the preliminary report the patient remained asymptomatic for approximately nine months. She then developed metastatic nodules in the skin of the neck and scalp. The postcervical lymph nodes became enlarged and hard. Roentgenograms made at this time revealed evidence of pulmonary metastasis and decalcification of the previously calcified osseous metastases.

Testosterone therapy was reinstituted and the patient received 25 mg. twice a week over a period of sixteen weeks. For the following four weeks she was given 200 mg. bi weekly and 100 mg. twice a week for the subsequent fifteen weeks. The total dosage since reinstitution of the therapy was 5,250 mg. of the androgen.

The patient reported to the hospital for a period of thirteen months from the time the testosterone therapy was instituted. Roentgenograms at the end of this period disclosed

the metastases to be predominantly osteolytic. The involvement was so extensive that little else but disease could be seen. She is now in the terminal stage of the disease.

The history of D. F. (Case 4 in the original group) will be recapitulated in greater detail because this patient's subsequent course presents some unusual features. A right radical mastectomy was performed in October 1944 at the Memorial Hospital. The pathologic finding was a grade 3 infiltrating duct carcinoma with no node involvement. She received a cycle of postoperative roentgen therapy to the right axilla. Menstrual periods were regular. She was asymptomatic for five months following operation and no evidence of disease was found at periodic examinations.

In March, 1945, she experienced excruciating pain in the left hip radiating down the thigh. Roentgenographic investigation disclosed an area of destruction in the left ala of the sacrum. Testosterone therapy was instituted 200 mg being administered daily for one week and 25 mg triweekly for the following ten weeks for a total of 1150 mg. Subsequently, treatment was continued with 25 mg twice a week for three months for a grand total of 2,750 mg.

The patient's pain diminished after two weeks of testosterone therapy. She was asymptomatic and had gained weight two months after the institution of the therapy. Roentgenograms in June and September, 1945, revealed progressive calcification in the metastatic area. She developed no other lesion. Amenorrhea had been present during this period. Therapy was discontinued in October, 1945. The patient had been asymptomatic for about six months and had continued to work during this interval.

One month after withdrawal of the testosterone the patient experienced an atypical menstrual period associated with discomfort in the left hip. A roentgenogram at this time revealed slight demineralization in the left wing of the sacrum. The pain in the left hip increased in intensity until at the end of a week it was excruciating. She could not eat, sleep, or walk. Her face was drawn and haggard. Large doses of codeine gave slight relief. The administration of 100 mg of the androgen on Nov. 6, 1945, was followed by amelioration of pain within twenty-four hours. Another injection of 100 mg two days later produced a further diminution of pain. For the ensuing week spotty vaginal bleeding occurred. The patient continued to receive 100 mg triweekly for a total dose of 1,400 mg since the resumption of the therapy. A roentgenogram taken at this time revealed evidence suggesting some bone regeneration in the area of destruction in the left ala of the sacrum. The patient again became asymptomatic and the therapy was discontinued.

Approximately five weeks later an irregular menstrual period which consisted of spotting for two days occurred. One week after the onset of the menses the patient again experienced pain in the left hip. Testosterone therapy was instituted this time without delay. Within twenty-four hours after an initial injection of 100 mg there was considerable diminution of the pain. Two additional treatments of 100 mg each were given on alternate days. At the end of one week she was asymptomatic. A roentgenogram made on Feb. 5, 1946, revealed further increase of calcification in the metastatic lesion of the sacrum.

After remaining asymptomatic for one month she experienced slight discomfort in the left hip. Menstruation began a few days later and the pain increased in intensity. The administration of 25 mg of testosterone propionate on three alternate days produced no diminution of the pain. One hundred milligrams were then given on alternate days, and after the third injection the patient was asymptomatic.

Comment—This patient is now in her second year of testosterone therapy, and has developed no further evidence of disease. She is asymptomatic as long as she is kept amenorrheic by the androgen. When testosterone propionate is withdrawn there is a return of the menses accompanied by agonizing pain in the hip. The patient cannot sit stand or lie sleep is impossible. These symptoms promptly disappear with the administration of 100 mg on three alternate days. Twenty-five milligrams on three alternate days do not influence

the pain. The size of the individual dose is evidently an important factor. To date there have been five episodes successfully controlled by testosterone therapy.

The remainder of this communication reports a new series of eleven cases of advanced carcinoma of the female breast with osseous metastases treated with testosterone propionate.

CASE 1—A. W. was a 60 year old white woman. In August, 1945, a left radical mastectomy was performed at the Memorial Hospital. The pathologic diagnosis was infiltrating duct carcinoma, grade 3, metastatic to the axillary nodes at all levels. No postoperative roentgen therapy was administered. She was twelve years postmenopause.

The patient remained asymptomatic and apparently free of disease for about three months. She then returned to the clinic because of extreme pain in the right hip and thigh. Radiologic studies disclosed extensive metastasis to the pelvis and upper end of the shaft of the right femur (Fig 1).



Fig 1 (Case 1) —Numerous areas of metastasis are seen in the neck and shaft of the femur.

Therapy—From Nov. 8, 1945, to Jan. 12, 1946, the patient received 200 mg. of testosterone propionate intramuscularly biweekly for a total dose of 3,600 mg. She received no other form of treatment.

Course—At the end of two weeks of treatment the pain had decreased in intensity. At the end of the third week she no longer had sharp pain and could sleep at night without taking codeine. Some soreness and stiffness in the right thigh persisted. At the end of the fourth week the pain had entirely disappeared. Roentgenographic studies in February,

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TABLE I LABORATORY DATA, CASE 1

	11/1/45	12/4/45	1/3/46 (THERAPY DISCON- TINUED)	2/21/46	3/12/46	4/4/46	5/20/46
Blood							
Hb	80	81				82	89
RBC	4.2	4.3				3.9	4.2
WBC	60	81				73	41
Polys	73	66				74	63
Monos.	2	4				2	3
Lymph	24	28				24	34
Alkaline phosphatase	37	53	76	80	80	50	70
Calcium	11.1	10.0	9.9	10.4	10.0	10.2	10.3
Chlorides	104	106	109	104	106	105	107
Phosphorus	3.84	3.16	2.90	3.96	2.82	3.26	3.86
Protein	66	65	66	70	77	69	69
Urine							
Sp Gr	1.014						1.020
Alb	0						0
Sugar	0						0
Micro	Occa. WBC.						0
Body weight (pounds)	159½	163½	164	155		157½	157



FIG. 2 (Case 1).—Roentgenogram made three months after the one shown in FIG. 1. During this period the patient received 3,500 mg. of testosterone propionate. The increased density produced by a deposition of calcium in the metastatic areas is well defined.

1946, revealed evidence of bone regeneration in the areas of destruction (Fig 2) Roentgenograms taken in May, 1946 revealed no significant interval change. The patient has remained asymptomatic to date (July, 1946).

Comment—The alkaline phosphatase exhibited a rise during the period that calcium deposition was demonstrated roentgenographically. Concomitant with the rise in phosphatase there was a drop in serum calcium. The elevation of the serum alkaline phosphatase continued after cessation of the androgen therapy. There was the customary increase in body weight which however, was not retained after the therapy was discontinued. These changes are represented by the curves in Fig 3.

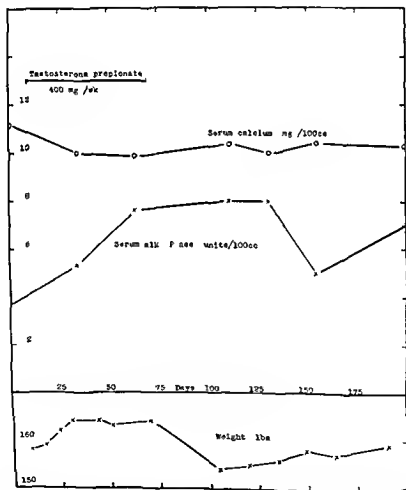


Fig 3 (Case 1)—Graphic representation of the alterations in the serum calcium and alkaline phosphatase concomitant with the roentgenographic changes depicted in Fig 2. There is a fall in the serum calcium and a rise in the alkaline phosphatase. The latter continues for a time after withdrawal of the testosterone. The initial body weight gain is lost after withdrawal of the androgen.

CASE 2—Y. P. was a 59 year-old white woman. She came to the Memorial Hospital in June, 1944, because of pain in the left arm. One year previously she had undergone a left radical mastectomy and postoperative roentgen therapy at another institution. Histologic study at the Memorial Hospital of a submitted slide of the tumor disclosed a comedo and infiltrating duct carcinoma, grade 2. Menses had ceased spontaneously when she was 57 years old.



Fig. 4 (Case 2)—Large areas of destruction are seen in the head, neck and shaft of the humerus.

Roentgenographic investigation in July, 1944, revealed evidence of metastasis to the head and neck of the left humerus. The patient received 1,200 r to the upper anterior and 800 r to the upper posterior aspect of the left humerus from July, 1944, to August 1944. The pain in the left shoulder subsided following irradiation but motion at the shoulder joint was markedly restricted. After remaining asymptomatic for about one year she returned in November, 1945, because of extreme pain in the left shoulder. There was associated muscle spasm. Radiologic examination Nov. 15, 1945, revealed evidence of metastasis in the shaft of the left humerus and of reactivation of the previous irradiated areas of metastases in the head and neck of this bone (Fig. 4).

Therapy—From Nov. 24, 1945, to Jan. 12, 1946, the patient received 200 mg of testosterone propionate biweekly for a total dose of 2,400 mg.

Course—Three weeks from the time testosterone therapy was instituted the pain and the muscle spasm around the left shoulder had diminished markedly. The function of the left arm and shoulder continued to improve and the patient was able to perform household

duties and work her truck garden. She was asymptomatic after six weeks of treatment and has so remained until the present time, a period of six months.

A roentgenogram of the left humerus taken in March, 1946, six weeks after cessation of the testosterone therapy was reported as showing recalcification in the previously described metastatic areas (Fig 5). There was no evidence that growth of the metastatic lesions had occurred since the previous roentgenogram was taken in November or that new areas of bone destruction had appeared.



Fig 5 (Case 2)—Roentgenogram was made 3½ months after the one shown in Fig 4. During this interval the patient received 2400 mg of testosterone propionate. Calcium has been deposited in all the metastatic areas. The cortex has regenerated in the head-neck and involved portion of the shaft.

Comment—This patient showed remarkable improvement. The body weight exhibited the usual rise during the androgen therapy and the drop when the treatment was withdrawn. There were no significant changes in the alkaline phosphatase such as were found in some of the other cases in the present series in which calcium deposition occurred. The testosterone therapy induced a deposition of calcium in a bone that had been previously irradiated. Although the amount of irradiation was small the results from the administration of the androgen would seem to indicate that previous irradiation of bone does not prevent it from recalcifying under the stimulus of the androgen.

TABLE II LABORATORY DATA, CASE 2

	11/15/43	12/15/43	1/19/46 (THERAPY DISCON- TINUED)	2/21/46	4/16/46
Blood					
Hb	78	82	82		68
R B C	39	38	39		33
W B C	61	56	98		60
Polys.	51	73	80		61
Monos	2	2			4
Lymph	46	25	20		33
Calcium	11.2	10.9	10.9	11.1	10.2
Chlorides	95	101	101	103	105
Alkaline phosphatase	30	25	31	42	34
Phosphorus	2.94	2.44	2.46	2.86	3.10
Protein	7.2	7.3	7.3	7.5	6.9
Urine					
Sp Gr	1006	1021			1020
Alb	0	1+			0
Sugar	0	0			0
Micro	Occa. R B C	Occa. R B C			Occa. W B C.
Body weight (pounds)	163	169½	171	162½	161

CASE 2—M K was a 39 year old white woman. In 1932 a left radical mastectomy was performed at another institution. The pathologic diagnosis at the Memorial Hospital of a submitted slide was infiltrating carcinoma simplex. The patient received a cycle of postoperative roentgen therapy at the Memorial Hospital. After remaining free of disease for five years (1937) she developed a metastatic nodule in the mastectomy scar. The nodule was excised at this institution. Histopathologic examination revealed it to be recurrent mammary carcinoma.

The patient remained free of disease for another period of six years (1943). At this time another nodule appeared in the mastectomy scar which regressed with radiation therapy administered at the Memorial Hospital.

In July, 1945, thirteen years after mastectomy the patient developed pain in the right shoulder. A roentgenogram made at the Memorial Hospital in October, 1945, disclosed areas

TABLE III LABORATORY DATA, CASE 3

	10/6/45	11/20/45	12/11/45	1/10/46	1/19/46	2/23/46	4/9/46
Blood							
Hb	76		93				62
R B C	3.5		4.5				3.1
W B C	4.5		60				66
Polys	64		59				80
Monos			2				1
Lymph	36		29				19
Alkaline phosphatase	38	62	38	42	37	36	42
Calcium		10.8	11.6		10.0	10.0	10.1
Chlorides		105	103			104	104
Phosphorus	3.44	2.02	3.16	2.98	2.48	3.09	3.32
Protein		7.1	7.3	8.1	7.6	7.5	7.7
Urine							
Sp Gr	1.015		1.016				1.016
Alb	0		Trace				0
Sugar	0		0				0
Micro	Epith		Occa. pos clump				0
Body weight (pounds)	189	196½	195½	190½	192	188	192½

of destruction in the head of the right scapula and in the right seventh rib (Fig 6). The lumbar spine and pelvis were negative for evidence of metastasis.

Therapy—The patient received 100 mg of testosterone propionate triweekly from Oct 9 to Nov 17 1945 for a total dose of 1300 mg. Treatment was continued with 25 mg administered triweekly from Nov 24 1945 to Jan 15 1946. From April 6, 1946, to June 8, 1946, an additional 600 mg were administered. The all-inclusive dose was 2475 mg. No other form of therapy was employed.

Course—After the first two weeks of treatment there was some diminution in the pain. At the end of the third week the pain had completely disappeared and she could move her arm freely. When the total dose had reached 1300 mg the patient complained of dizziness. Examination revealed some puffiness about the eyes and moderate pretibial edema. Because of this reaction the dose was reduced to 25 mg triweekly. The dizziness and edema promptly subsided. There was at no time any return of the pain.



FIG 6 (Case 3)—The head of the scapula is almost completely involved by the metastatic process. There is a small area of destruction in the seventh rib.

Radiographic studies made in January, 1946, three months after the institution of the androgen therapy revealed pronounced recalcification of the metastatic areas in the right scapula and right seventh rib (Fig 7). Testosterone therapy was withdrawn and the patient remained asymptomatic for the following three months. Then the pain in the right shoulder recurred. A roentgenogram taken April 9 1946 revealed that the calcified area of metastasis in the head of the scapula had become a little more osteolytic. Studies of the lumbar spine and pelvis revealed evidence of metastasis. There were however no symptoms referable to these regions. Testosterone therapy was again instituted and the patient became asymptomatic within three weeks.

TABLE II LABORATORY DATA CASE 2

	11/15/45	1/1/46	1/10/46 (THIRTY DAYS ON THERAPY)	1/14/46	4/16/46
Blood					
Hb	5	8	5		69
Ht R C	39	38	39		33
W B C	61	51	8		60
Polys	51	23	41		61
Monos		2			4
Lymph	13	2	20		33
Calcium	11.6	10.4	10.9	11.1	10.4
Chlorides	13	101	131	103	10
Alkaline phosphatase	74	7	31	42	34
Thyroxine	2.94	2.41	2.41	2.4	3.10
Iodine		73	73	75	9
Urine					
Hg Gr	1000	1001			10.0
Alb	0	14			0
Sugar	0	1			0
Mier					
Body weight (pounds)	Occa R B C	Occa R B C	11	101	Occa W B C
	16	194			161

CASE 1—M. H. was a young girl 11 years old. In 1941 she had a mastectomy was just made at another hospital. The pathologic diagnosis at the Memorial Hospital in 1941 was infiltration, carcinoma. The patient received a cycle of postoperative roentgen therapy at the Memorial Hospital. After remaining free of disease for five years (1946) she had a relapse of the carcinoma in the metastatic area. The node was excised at the hospital. Histologic examination revealed it to be recurrent carcinoma.

The patient in 1946 had another period of therapy (1947). At this time another relapse appeared in the metastatic area with a relapse of the carcinoma in the metastatic area.

In July 1947, the patient had a relapse of the carcinoma in the right side. A roentgenogram at the Memorial Hospital in October 1947 showed areas

TABLE III LABORATORY DATA CASE 3

	10/14/45	11/1/45	10/11/45	1/10/46	1/1/46	1/14/46	4/16/46
Blood							
Hb	70		93				69
Ht R C			45				31
W B C	45		60				68
Polys	61		59				60
Monos			2				4
Lymph	16		39				33
Alkaline phosphatase	78	6	38	10	37	37	40
Calcium		1.8	11.6		10.0	10.0	10.1
Chlorides		103	103			101	104
Thyroxine	3.44	6.0	3.16	2.08	2.48	2.09	3.30
Iodine		71	73	81	76	77	77
Urine							
Hg Gr	1015		1016				1016
Alb	0		Trm				0
Sugar	0		0				0
Mier	1 pH		Occa pas clump				
Body weight (pounds)	180	1904	1904	1904	190	188	1904

Roentgenographic investigation revealed irregular areas of bone destruction in the skull suggestive of carcinoma metastasis and evidence of metastasis to the twelfth dorsal and lumbar vertebrae

Therapy—Testosterone therapy was instituted on Jan 24, 1946. The patient received 100 mg of the androgen bi weekly for a total dose of 1,000 mg. No other type of therapy was employed.

Course—At the end of the third week of treatment the patient's back pain had regressed markedly. She was able to walk and to flex the spine with very little discomfort. There was continued symptomatic improvement during the five week period that the patient attended the clinic. She then failed to return for one month. Examination at the end of this interval revealed the exophthalmos to be present but the patient was asymptomatic.

Roentgenograms made in April, 1946, revealed the metastases in the lumbar and dorsal vertebrae to be predominantly osteoblastic with several dense structureless areas of bone present in the second and sixth lumbar vertebrae. Chemical studies revealed a rise in the alkaline phosphatase.

Comment—Despite radiologic castration this patient developed osseous metastases. There was a prompt response to testosterone therapy. Although the androgen was withdrawn after five weeks the serum alkaline phosphatase continued to rise. It would appear that the stimulus initiated by the androgen continues after its withdrawal.

TABLE IV LABORATORY DATA, CASE 4

	1/26/46	2/26/46 (THERAPY DISCONTINUED)	4/16/46
Blood			
Hb	62		
RBC	32		
WBC	50		
Polys	67		
Monos	5		
Lymph	28		
Alkaline phosphatase	51	70	85
Calcium	10.2	11.1	11.0
Chlorides	103	104	106
Phosphorus	3.48	2.55	3.84
Protein	8.6	7.9	8.1
Urine			
Sp. Gr.			1.012
Alb.			0
Sugar			0
Micro			
Body weight (pounds)		152	Occa WBC 142

CASE 5—M. B. was a 55 year old white woman. In 1944, a right radical mastectomy was performed at another institution. The pathologic finding was an infiltrating duct carcinoma, grade 3. Three years after the operation the patient developed pain in the lower back and hips. Roentgenograms taken at this time disclosed metastatic disease in the lumbar spine, pelvis, and upper femora.

In June, 1945, at another institution, the patient received 1,255 r to the posterior pelvis and 415 r to the lumbar spine with amelioration of the pain. The voltage employed was 400 kv. The pain recurred in October, 1945, and, at the same institution, the patient received 1,250 r to the left hip and thigh anteriorly and 210 r to the right hip posteriorly. The pain persisted, therefore an additional 810 r. were administered to both femora in November, 1945. The patient obtained no relief.

Comment—Metastasis which developed in the scapula thirteen years after mastectomy yielded satisfactorily to testosterone therapy. The lesion became reactivated and pain recurred when the androgen was withdrawn. Reinstitution of the therapy caused a disappearance of the pain.



Fig. 7 (Case 3)—Roentgenogram taken three months after that shown in the previous figure reveals the pronounced calcification that has taken place in the metastatic lesions. The patient had received 1750 mg. of testosterone propionate during this period.

CASE 4—M. W. was a 43 year old colored woman. In March, 1945, a right radical mastectomy was performed. The pathologic report was infiltrating duct carcinoma. Menstruation was regular.

One month after operation the patient experienced pain in the left hip. Roentgenographic studies of the lumbar spine and pelvis failed to reveal evidence of metastasis. The pain was attributed to the high grade of malignancy of the tumor. The suggestive pain in the hip made this

The pain in the hip subsided following castration and the patient remained asymptomatic for six months. She returned to the clinic in June, 1946, with pain in the ribs and of inability to move the head and neck. There was pronounced left exophthalmos.

TABLE VI LABORATORY DATA, CASE 6

	10/15/45	12/20/45	1/17/46	2/17/46	3/28/46	4/25/46
Blood						
Hb	56	60	58		65	
R.B.C	29	28	32		30	
W.B.C	53	56	54		40	
Polys	71	68	56		67	
Monos	2	1	2		1	
Lymph	23	31	40		31	
Alkaline phosphatase	84	147	127	101	108	44
Calcium	110	107	99	101	104	111
Chlorides		104		105	106	102
Phosphorus	398	300	324	364	376	384
Protein		62	64	62	69	68
Urine						
Sp. Gr	1.012				1.022	
Alb	Trace				Trace	
Sugar	0				0	
Micro	Occa. W.B.C				Occa. R.B.C	
Body weight (pounds)	128	133	135	137½	131½	

Therapy—Testosterone therapy was instituted on Nov. 6, 1945. The patient received 200 mg. of the androgen twice a week over approximately twelve weeks for a total dose of 3,200 mg. There were two absences of about two weeks each from the clinic during this period. Following this she received 25 mg. twice a week for seven weeks for an additional dose of 375 mg. The dosage was then increased to 200 mg. twice a week for a period of six weeks for a grand total of 6,175 mg.

Course—The patient was asymptomatic at the end of one month of therapy and maintained this status for four months. She then developed a sensation of numbness over the left side of the mandible. Roentgenograms of the mandible and skull at this time revealed metastases predominantly osteoblastic, to the vault of the skull. At this time the dose was increased from 25 to 200 mg. biweekly. Roentgenograms of the chest, lumbar spine, pelvis, and right shoulder girdle were taken at monthly intervals from October, 1945, to June, 1946. A slight increase in the number and extent of the osseous metastases which became more osteoblastic in character was noted. Aside from a sensation of numbness in the region of the chin the patient has been asymptomatic for seven months.

Comment—Irradiation did not appreciably influence the pain. The administration of testosterone was followed by a rise in the serum alkaline phosphatase and a disappearance of the pain. The metastases became more osteoblastic in character which may account for the subsidence of the pain.

TABLE VII LABORATORY DATA, CASE 7

	7/31/45	9/27/45	10/15/45	11/15/45	12/11/45
Blood					
Hb	75	69	65	76	
R.B.C	35	34	32	34	
W.B.C	43	65	76	65	
Polys.	46	33	58	41	
Monos	1	3	6	2	
Lymph	53	61	36	57	
Alkaline phosphatase	47	98	131	89	52
Calcium	111	111	99	98	101
Chlorides				103	99
Phosphorus	381	220	226	234	286
Protein				68	71
Urine					
Sp. Gr		1.018			
Alb		Trace			
Sugar		Trace			
Micro		Many R.B.C			
Body weight (pounds)	125	130½	132½	130½	124

Therapy and Course—Beginning Dec 1, 1915, at the Memorial Hospital the patient received 100 mg of testosterone propionate daily for a total dose of 1,200 mg. She was then able to walk up and down stairs unaided whereas two weeks previously she had entered the hospital in a wheel chair.

She returned to her home in a distant city where she continued to receive 100 mg of the androgen six days a week for three weeks. Treatment was then continued with 25 mg tri weekly until May 7, 1916, for a grand total of 4,150 mg since the institution of the androgen therapy in December.

Röntgenographic studies at the Memorial Hospital in June, 1916, revealed a slight increase in the extent of the metastases observed in previous roentgenograms. They were however, slightly more osteolytic in character. Some stiffness persisted in the hips but there was no pain.

Comment—Testosterone produced striking relief of pain after irradiation was no longer effective. Repeated blood chemical studies revealed a progressive elevation of the serum alkaline phosphatase. The patient developed a progressively severe anemia which was probably due to the suppression of hematopoiesis by metastases in the long bones.

TABLE V LABORATORY DATA, CASE 5

	11/25/45	12/13/45	2/19/46	3/1/46
Blood				
Hb	69	75		58
R.B.C.	3.5	3.7		3
W.B.C.	68	52		47
Polys	78	76		62
Eosin.		2		
Monos.	4	10		8
Lymph	18	12		23
Immature forms				7
Alkaline phosphatase	38	52	64	94
Calcium	10.4	10.2	10.8	12.1
Chlorides	97	103	101	101
Phosphorus	4.30	3.30	4.22	4.70
Protein	6.5	6.5	7.0	7.2
Urine				
Sp. Gr.	1.020	1.010		
Alb.	0	0		
Sugar	0	0		
Mier.	Occa. R.B.C.	Neg.		

CASE 6—H. K. was a 40-year-old white woman. In December, 1943, a radical mastectomy for infiltrating duct carcinoma, grade 3, was performed at the Memorial Hospital. She received a cycle of post-operative irradiation because the axillary lymph nodes were involved. Menstrual periods were irregular at the time of operation and shortly thereafter she underwent a spontaneous menopause.

The patient began to experience pain in the lumbar region radiating down the thighs in March, 1945, more than one year following operation. Roentgenograms revealed evidence of metastasis to the lumbar spine and pelvis. In April, 1945, the right side of the pelvis received 800 r to each of three ports, an anterior, a posterior, and a lateral. In June, 1945, 1,200 r were administered to the lumbar spine and sacrum and in July, 1945, 400 r to each of two anterior and 800 r to each of two posterior pelvic ports. The voltage employed was 250 kv. There was some diminution of the pain following roentgen therapy. It soon became severe again. Later she developed pain in the ribs and right shoulder. Roentgenograms taken October, 1945, of the right shoulder and the chest revealed widespread metastases to practically all of the ribs, the vertebrae, and the right humerus and glenoid fossa.

roentgenogram made Nov 24, 1945 disclosed no significant change upon comparison with that taken in July, 1945

In December, 1945, four months after the institution of the testosterone therapy numerous skin nodules were observed throughout the scalp. An excisional biopsy of one of the nodules was reported as metastatic mammary carcinoma. A roentgenogram of the lumbar spine and pelvis taken at this time revealed the degree of involvement to be somewhat more extensive and the lesions somewhat more osteolytic in character than at the examination in November, 1945. The patient failed to return to the clinic and upon investigation it was found that she had developed pulmonary metastases.

Comment—Although there was a striking rise in the serum alkaline phosphatase (Fig 8) there was no roentgenologic evidence of calcification in the osseous metastases. Subsequently, there was a slight increase in the osteolytic character of the lesions. The patient's condition deteriorated rapidly after the appearance of pulmonary metastases.

CASE 8—G W was a 55 year old white woman. In July, 1946, a right radical mastectomy was performed at another institution. She came to the Memorial Hospital six months later because she noticed some "lumps" in the right axilla. Menopause had occurred ten years previous to the mastectomy.

Examination in January, 1946, revealed several subcutaneous nodules in the right axilla. An excisional biopsy of one of these nodules was reported as metastatic mammary carcinoma. Roentgenograms disclosed numerous areas of metastasis in the lumbar vertebrae, the pelvis, and the upper end of the left femur. There was no evidence of metastasis to the lungs. The patient was asymptomatic.

Therapy—Testosterone therapy was instituted on Feb 2, 1946. Relatively small doses of the androgen, 50 mg biweekly, were employed because the osseous lesions were causing no symptoms. In addition 5 Gm of calcium gluconate and 20 drops of vitamin D were taken daily by the patient during the period of therapy. The androgen was administered over a period of thirteen weeks with occasional lapses, for a total of 1,150 mg.

Course—The patient developed severe pain in the left hip two weeks after the androgen therapy was instituted. Despite considerable pain she returned for treatment after one week's absence. Roentgenographic studies at this time revealed an increase in the size and extent of the metastatic lesions. After three weeks of additional testosterone therapy the

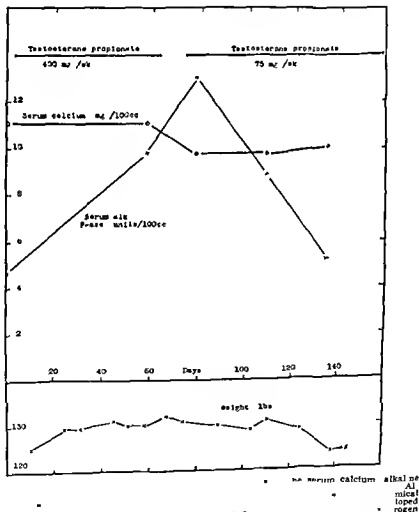
TABLE VIII LABORATORY DATA, CASE 8

	1/31/46	3/5/46	4/2/46	4/30/46
Blood				
Hb	79	74		72
RBC	4.0	3.6		4.1
WBC	7.7	6.2		12.6
Polys	47	63		53
Eosin	1	3		
Monos	2	2		6
Lymph	50	33		36
Alkaline phosphatase	4.5	5.5	6.2	10.1
Calcium	11.7	12.2	10.7	11.4
Chlorides	103	107	106	102
Phosphorus	3.62	3.61	3.06	3.54
Protein	6.6	6.9	6.7	7.2
Urine				
Sp Gr	1.004			1.000
Alb	0			1+
Sugar	0			0
Micr	0			0
Body weight (pounds)	137	140	143	Occa casts 139

CASE 7—D M was a 45 year old white woman. In January, 1940, a right radical mastectomy for a grade 2 infiltrating duct carcinoma was performed at the Memorial Hospital. There was no axillary lymph node involvement. For over five years she was asymptomatic and apparently free of disease. She then developed pain in the lumbar spine. Roentgenograms taken July, 1945, revealed evidence of extensive metastasis to the lumbar spine and pelvis. Menstrual periods were regular.

Therapy—Testosterone therapy was instituted on Aug 7, 1945. For a period of two months 200 mg of the androgen were administered biweekly for a total dose of 3,200 mg. Treatment was then continued with 25 mg triweekly for an additional six weeks until a grand total of 3,650 mg had been administered.

Course—At the end of the first month of treatment the patient was asymptomatic aside from occasional discomfort and stiffness in the left hip when climbing stairs. A



this time revealed a hypercalcemia therefore the androgen therapy was terminated. One week later a further elevation of the serum calcium was found. The nausea and vomiting were uncontrollable. The patient's condition was so poor that she was institutionalized.

Comment—This case differs from the previous one in that the reactivation of the lesions occurred after the androgen had been withdrawn. The serum calcium continued to rise despite cessation of testosterone therapy which is contrary to our previously reported findings¹ and to those of Farrow and Woodard.²

CASE 10—A K was a 62-year-old white woman. In 1942, a right radical mastectomy was performed at the Memorial Hospital. The pathologic diagnosis was a gelatinous adenocarcinoma, grade 2, nodes clear. The patient was apparently free of disease for about three years. She then developed pain in the cervical region and the right hand. Roentgenograms taken in May 1943, revealed metastasis to the cervical vertebrae but no evidence of involvement of the bones of the hand. She was given 1,000 r high voltage x irradiation to the cervical region with some diminution of the pain. The pain and the swelling in the right hand increased. Roentgenograms taken in July 1943, revealed evidence of destruction of the right fourth metacarpal consistent with metastasis.

Theapy—Testosterone therapy was instituted Aug. 2, 1943. The patient received 200 mg biweekly for seven weeks for a total dose of 2,800 mg.

Course—The swelling and pain in the right hand grew progressively worse. She developed a lesion on the scalp which was presumably metastatic mammary carcinoma. The patient died of the disease one week after the termination of the androgen therapy.

CASE 11—A R was a 53-year-old white woman. In 1941, a left radical mastectomy was performed at the Memorial Hospital. The pathologic examination revealed infiltrating duct carcinoma, grade 2, no lymph node involvement. Roentgenographic studies of the chest, lumbar spine and pelvis were negative for evidence of metastasis.

Following the operation the patient remained apparently in good health for about four years. In May 1945 during the course of a routine checkup at the Memorial Hospital left subclavicular nodes were palpable. An aspiration biopsy was reported as carcinoma. The palpable nodes disappeared completely with roentgen therapy. The patient remained asymptomatic for approximately six months. She then developed pain in the right side of the chest. Roentgenograms taken in October 1945, revealed areas of metastasis in the dorsal spine and ribs.

Therapy—From Nov. 1, 1945, to Jan. 31, 1946, the patient received testosterone propionate biweekly for 12 weeks for a total dose of 2,400 mg. The therapy was discontinued March 7, 1946, because of side effects.

Course—Two weeks after the institution of testosterone therapy the patient was asymptomatic and returned to work. She had occasional discomfort in the left hip. Roentgenograms taken Jan. 15, 1946, revealed the metastases to be a little more extensive but more sclerotic in character. Five months after the androgen therapy was discontinued she

TABLE X LABORATORY DATA, CASE 11

	10/25/45	11/27/45	1/10/46	2/19/46
Calcium	11.3	10.6	10.9	11.0
Chloride		101		100
Alkaline				
Phosphatase	50	52	85	97
Phosphorus	3.96	2.63	2.93	3.22
Protein		6.6	7.2	7.4
Body weight (pounds)		163	165	162½

pain disappeared and she remained asymptomatic for one month. She then developed a cough. A roentgenogram revealed a large amount of fluid in the left side of the chest and metastatic lesions in two ribs. The lesions in the pelvis were essentially unchanged. Shortly after she failed to return to the clinic.

Comment—This case is unusual in that the androgen at first appeared to activate the lesions and later to inactivate them. The activation by the androgen is apparently similar to the phenomenon described by Farrow and Woodard.²

CASE 9—J. L. was a 39 year old white woman. In June, 1944, a right radical mastectomy was performed at the Memorial Hospital. The pathologic diagnosis was comedo and infiltrating duct carcinoma grade 3. She received a postoperative cycle of roentgenotherapy to the right axilla. Menstrual periods were regular.

There was no evidence of recurrent disease for almost two years. The patient then began to experience pain in the left shoulder and lower back and was unable to flex the lumbar spine. Roentgenograms taken in March, 1946, revealed evidence of metastasis to the twelfth thoracic and fifth lumbar vertebrae, to the shafts of both femora and to the glenoid fossa of the left scapula.

Therapy—From March 30, 1946, to May 15, 1946, she received 50 mg of testosterone propionate biweekly for a total of 400 mg. From June 11, 1946, to June 14, 1946, she received three injections of 100 mg each for a grand total of 300 mg. No other type of therapy was employed.

Course—Within one month from the time androgen therapy was instituted she was asymptomatic, able to flex the lumbar spine without discomfort and wished to return to work. Roentgenograms at this time, April 30, 1946, revealed increased density in the previously described areas of destruction in the right upper femur and in the left scapula.

The patient remained asymptomatic for one month during which no therapy was administered. Then the pain in the lower back recurred associated with nausea and vomiting. Abdominal examination failed to reveal any palpable viscera or masses. Roentgenologic studies made June 8, 1946, revealed an increase in the size and extent of the osseous metastases. Blood chemical studies disclosed a suggestive elevation of the serum calcium.

Shortly thereafter the patient reported bloody vaginal spotting. This was the first menstrual period since the institution of androgen therapy ten weeks previously. The vomiting continued and the back pain became progressively worse. Therefore, 100 mg of testosterone propionate were administered on alternate days for three doses. The vaginal bleeding ceased but the pain, nausea and vomiting became accentuated. Blood chemical studies at

TABLE IV. LABORATORY DATA, CASE 9

	3/18/46	4/23/46	5/12/46	6/11/46	6/18/46	6/22/46
Blood						
Hb	80		73			
RBC	3.8		3.6			
WBC	3.4		4.1			
Polys	63		57			
Monos	1		3			
Lymph	36		40			
Alkaline phosphatase	68	54	59	58	46	63
Calcium	11.0	10.4	10.5	12.1	13.4	15.0
Chlorides	105	111	111	100	100	
Phosphorus	3.50	2.61	3.62	3.56	4.46	4.66
Protein	7.1	6.9	7.0	7.3	7.1	7.7
Urine						
Sp. Gr.	1.016					
Alb.	0					
Sugar	0					
Micro	Neg					
Body weight (pounds)	115	115½	115½		103½	

The androgen induced amenorrhea but the menses returned after this therapy was withdrawn. One patient who was asymptomatic as long as she was kept amenorrheic by testosterone propionate developed pain in the metastatic area when the androgen was withdrawn and the menses returned. In some patients acne appeared on the neck, shoulders and chest. The other undesirable sequelae were facial hirsutism and deepening of the voice. In one patient there was transient edema of the face and legs. An increase in libido was noted in many patients.

All of the patients exhibited a gain in body weight during the initial period of androgen medication. When the therapy was terminated much of this weight was lost. The gain in weight was probably due to protein nitrogen retention by the tissues rather than to fluid retention.³ In the majority of cases there was no significant alteration in the blood serum protein chlorides or urine to judge by routine examinations.

From the results obtained in the present investigation it would appear that testosterone propionate is of value in the treatment of osseous metastases secondary to carcinoma of the female breast.

The authors acknowledge their indebtedness to the Schering Corporation, Bloomfield, N. J. for the testosterone propionate (Oreton) used in this investigation.

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began to have abdominal pain. Upon examination an enlargement of the liver evidently due to metastases, was found.

Comment—There was an elevation of serum alkaline phosphatase concomitant with osteoblastic changes in the metastases. The change in the character of the metastases may be the factor that caused a diminution in the pain. The general condition of the patient deteriorated rapidly after the onset of the liver enlargement.

SUMMARY AND CONCLUSIONS

Since the preliminary report on the use of testosterone propionate in advanced carcinoma of the female breast, eleven additional patients with osseous metastases have been treated with the androgen. These patients ranged in age from 39 to 62 years. With three exceptions they were treated exclusively with testosterone propionate administered intramuscularly. The exceptions were patients in whom previous irradiation of osseous metastases had failed to control the pain. In so far as these patients improved with subsequent androgen therapy it would seem that repeated irradiation of bones does not destroy their power to react to the androgen.

Symptomatic improvement, evident within two weeks after the institution of the therapy, was manifested in eight patients. Six patients revealed roentgenologic evidence of calcification in the metastatic areas. In some patients these changes were discernible four to six weeks after institution of the therapy. In some instances as bone density increased there was a drop in the serum calcium indicating either a deposition of this element in the metastatic areas or a decrease in osteolysis. There was a rise in the serum alkaline phosphatase in eight patients. In the absence of liver disease an elevation in serum alkaline phosphatase indicates bone growth or an attempt at bone regeneration. It appears likely that, during the period of imbalance following the institution of endocrine therapy, some mechanism perhaps involving the pituitary or the suprarenal stimulates osteoblastic activity and alkaline phosphatase production.

The bone lesions appeared to remain quiescent for a variable length of time after the androgen therapy was terminated. If pain recurred it could be controlled by additional androgen therapy. It would appear that in many instances a favorable status may be maintained until pulmonary or liver metastasis appears. When this occurs the patient rapidly retrogresses and dies within a relatively short time despite the continued administration of the androgen.

The favorable results in the present series have been obtained with smaller amounts of testosterone propionate than were used in patients previously reported.¹ The dosages employed successfully in the present investigation were 100 and 200 mg biweekly and 100 mg triweekly. It is suggestive that the least satisfactory results were obtained when biweekly doses of 50 mg were employed. The treatment was usually continued until the patient became asymptomatic. It is probable that therapy can be terminated before this point is reached and yet have the symptomatic improvement and the rise in the alkaline phosphatase continue.

father or mother had any difficulty with the back or whether they had noted the presence of brownish or blackish coloration of the urine. There were no other living members of the family.

On physical examination it was noted that this soldier walked with a definite limp. The trunk was stooped slightly forward and this resulted in an obliteration of the lumbar lordosis. A diffuse ruddiness of the face and a slate-colored pigmentation of the auricles were observed. No gross discoloration of the cornea or sclera was present. The orthopedic examination revealed that the range of flexion of the trunk was possible to an angle of 120 degrees. Extension of the trunk was restricted to the neutral or vertical plane. Tenderness was experienced on pressure over the lumbosacral area. A 15 degree restriction was encountered to straight leg raising on the right as well as on the left lower extremities. There was also a 10 degree restriction to complete flexion of the right thigh. Internal rotation of either thigh was possible only to the neutral plane. Combined or total abduction of the thighs was not impaired.

Examination of the knees revealed the absence of any effusion. Crepitation was felt and heard in both knees but to a greater extent on the left side. Direct pressure made over the left patella caused discomfort and tenderness. The left leg could be actively extended to an angle of 180 degrees and flexed to an angle of 50 degrees. These movements caused pain in the left knee joint. The right knee presented a normal range of motion.

Examination of the ankles revealed a thickening of the left tendo achillis at a level of about one inch proximal to its attachment to the os calcis. The range of motion at the ankles was within normal limits. As far as the upper extremities were concerned, 15 degrees restriction in motion was noted to complete abduction of the arms in the coronal plane. Otherwise, the other joints of the upper extremity revealed nothing unusual.

The pulsations of the radial dorsalis pedis, and posterior tibial arteries were palpable. There was no evidence by palpation of any calcification of these blood vessels. Ophthalmoscopic examination revealed that the optic disc and retina were normal in appearance. Slit lamp examination demonstrated the presence of brownish black small accumulations of pigment in the stroma of the bulbar conjunctiva of the left eye at the region of nine o'clock. This pigment was deposited in two rows about 3 to 4 mm. from the limbus. A few of the deposits were of macroscopic size. A single deposit was found in the conjunctiva of the right eye at the region of nine o'clock.

Radiograph examination of the vertebral column disclosed narrowing and calcification of the intervertebral regions of the dorsal and lumbar vertebrae (Fig 1). These foci of calcification did not project beyond the limits of the anterior ligaments. There were several small marginal exostoses noted in these vertebral bodies, but no evidence of ossification of the anterior ligaments or ankylosis of the facets. Calcification of the interpubic ligaments was present.

Radiographic examination of the knees disclosed a marked irregularity and sclerosis in the subchondral region of the left patella and of the contiguous femoral articular surface. Small osteophytes were seen on the periphery of the articular surfaces of the tibia and femur of both knees. Several free roundish bodies were noted in the posterior compartment of the left knee (Fig 2). No free bodies were seen in the right knee joint. Radiographic examination of the shoulder areas revealed a subchondral erosion on the glenoid portion of the left scapula. No calcification of the labrum of the glenoid was noted.

Study of the peripheral blood revealed a hemoglobin of 120 per cent (Sahli), a red cell count of 6 million per cubic millimeter and a white count of 7,250 per cubic millimeter. The differential count showed a normal percentage distribution of the white cells. The hematocrit reading was 51 per cent. The erythrocyte sedimentation rate was 0 mm during the first hour.

Examination of the urine revealed that it was of yellow color, with a specific gravity of 1.012. The tests for albumin and sugar were negative. When the urine was left exposed

*Occasionally the radiographic picture of the vertebral column may simulate that noted in von Bechterew's disease.

ALKAPTONURIC ARTHRITIS

CAUSE FOR FREE INTRA-ARTICULAR BODIES

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AN UNUSUAL cause for the formation of free bodies in a joint cavity is a disturbance in the catabolism of the proteins tyrosine and phenylalanine. In patients with this disorder, these proteins which are present in food and tissues are not completely metabolized and form an intermediate product known as *homogentisic acid*—an alkaptan body. This abnormality in metabolism known as *alkaptonuria* may be due to an inborn error of catabolism of proteins or to prolonged use of phenol dressings for ulcers or wounds. The *homogentisic acid* which is deposited in tissues and excreted in the urine causes the color of the urine to change to brown or black on exposure to air. Associated with the formation of this acid there is a tendency either for conversion of these alkaptan bodies into pigment *in situ* or for a deposition of other pigmented granules into either relatively avascular tissues or into those with poor metabolism.¹ Thus the articular cartilage, tendons, ligaments, intervertebral discs, fibrocartilage, *sclerose atherosclerotic plaques*, etc., may become pigmented resulting in a condition known as *ochronosis*. Such depositions have also been known to occur in epithelial cells and in smooth striated and cardiac muscle. For some unknown reason when musculoskeletal tissues are the seats of such pigment deposition calcification or ossification may also occur at these sites. The articular cartilages, intervertebral discs, and other cartilaginous or ligamentous tissues may become calcified or ossified or may undergo prematurely, occasionally as early as childhood, degenerative changes commonly seen in ordinary osteoarthritis.² When the arthritic process affects the knee or any other large joint there may be an associated formation of free bodies in the articular cavity.³

This paper is presented in order to record the case of a patient who had free bodies in one of the knees as a result of this error in metabolism.

CASE REPORT

A 42 year old soldier was admitted to this hospital because of a pain in the left knee for thirty days. One month prior to this visit to the institution the patient slipped on the ice and twisted the left leg. The left knee became very painful and enlarged to a degree which interfered with locomotion. For this reason he was admitted to the hospital for treatment. On further questioning the patient stated that he had had pain in the lower back for the past five years. During this period of time he could not fully bend the trunk or lift heavy objects without experiencing local pain. He occasionally suffered from sprains in the ankles but had never had any severe pains or swellings of any of the joints of the upper or lower extremities. After the completion of the physical examination the patient was questioned about the color of the urine. He stated that for the past five years the urine had turned brownish black when it was exposed to the air. He denied the use of carbolic acid dressings or ointments. As for family history he did not know whether his

examination of the peripheral blood disclosed normal amounts of sugar, nonprotein nitrogen, cholesterol, calcium, phosphorus and alkaline phosphatase.

As surgical intervention was not indicated no histologic studies could be made of the free bodies in the left knee. However on the basis of the chemical findings in the urine and the radiographic examination of the skeleton it was felt that the changes in the knee joint were part of the picture of alkaptonuric arthritis. The soldier was returned to civilian life.



Fig. 2.—Lateral view of the knee reveals several free bodies in the posterior compartment. Note the increase in density in the subchondral region of the patella and of the contiguous femoral articular surface.

DISCUSSION

It is believed that articular cartilage is prematurely degenerated when homogentisic acid is deposited in it. Such cartilage becomes highly friable, easily cracked, and is separated readily from the subchondral zone. These detached portions of articular cartilage may then either be deposited on the synovial lining or lie freely in the articular cavity. The articular cartilages and their free fragments may become pigmented and are prone to further degeneration and calcification because of a secondary disturbance in the metabolism or nutrition of the cartilages. These detached islands of cartilage form the nidus for the free bodies found in association with alkaptonuria and ochronosis. Furthermore, the semilunar cartilages of the knee may also become pigmented and calcified, particularly if they are scarred or fibrotic. The modified or frayed articular cartilages in general predispose to a premature secondary generalized osteoarthritis with all of its well-known complications. In a like manner the deposition of pigment and cartilaginous plaques on the synovial lining causes a proliferative villous synovitis. Of interest is the reported finding of osteoporosis in association with ochronosis.⁷

In considering some of the various other causes for abnormal coloration of tissues in association with arthritis, one must think of melanuria, chronic argyria, methemoglobinemia, hemochromatosis, porphyria, carotinemia, Gaucher's disease, chloroma, neurofibromatosis, and fibrous dysplasia.

The predilection of the ochre pigment for the articular cartilages and the intervertebral tissues is of interest because a deposition of bile pigment in

to the air, it turned dusky brown. With the addition of a few drops of a solution of 5 per cent sodium hydroxide, the urine turned black on exposure to air. This reaction took place very readily when a current of air was passed through the alkalinized urine. Furthermore the alkalinized urine produced an immediate black discoloration when it was applied to the surface of photographic contact print paper in daylight. This test is considered by Eisberg to be specific for alkaptonuria. Alkaline extracts of the patient's hair, fingernails, saliva, stool, lacrimal secretion, and sweat failed to show this reaction on contact with photographic paper on exposure to daylight. Homogentisic acid was present in the urine and one study revealed the amount of 4.4 Gm. over a twenty-four hour period. The chemical



FIG. 1.—A. Lateral view of the dorsal vertebrae shows dense or opaque foci in the intervertebral regions. B. Anteroposterior and lateral views of the lower dorsal and of the lumbar vertebrae show similar changes.

ARTERIOSCLEROTIC ISCHEMIC NECROSIS OF THE LOWER EXTREMITIES

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THE operative mortality in patients with arteriosclerotic occlusion of the vessels of the lower extremities is still unreasonably high. This is true in spite of the excellent contributions by many authors who are interested in this field of surgery.^{1,2} The reported mortality has shown a reduction during the past decade from 30 to 40 per cent to 10 to 20 per cent. The improvement in surgery of peripheral arteriosclerosis has been largely accomplished by the following factors. In diabetic patients close cooperation between the medical and surgical attendants has been shown by McKittick³ to be of the utmost importance in the pre and postoperative regulation of the patient's disordered metabolism. The recognition of an adequate arterial supply in the presence of infection may preserve many extremities by the adoption of conservative therapy. Penicillin and the sulfonamides are useful in the control of spreading infection provided the blood supply is adequate. The correction of preoperative dehydration, acidosis and hypoproteinemia has rendered many patients better operative risks. A guillotine amputation performed as an emergency procedure has undoubtedly reduced the mortality in the presence of spreading infection. The release of sympathetic vasomotor control before ischemic necrosis has occurred promises to save many arteriosclerotic extremities.^{4,5} The arteriosclerotic patients who are candidates for sympathetic intervention must be selected carefully. It is well known that when the management of any disease is placed in the hands of one or two men who are interested in the details of diagnosis and therapy the results improve. The mortality is still sufficiently high however to warrant intensive study of the various factors that contribute to the postoperative death of these patients.

It seemed to me that an unusually large number of preliminary or minor toe amputations had been performed at University Hospitals during the past twelve years. To determine the frequency with which thigh amputation was preceded by toe amputations and the effect upon mortality the following statistics were compiled.

Only patients with arteriosclerotic occlusion of the peripheral arteries were included. Although some of these patients had superimposed pyogenic infection the main cause of disability was ischemia in every instance. Those patients who had amputations for severe infection in the presence of a clinically adequate arterial blood flow were excluded. The major amputations consisted of transection at either the mid femoral or the supracondylar level. No Gritti Stokes Callender transtibial or transmetatarsal amputations were performed. The minor amputations consisted of removal of one or more toes and in most

similar sites was observed in experimental studies of mice. Histologic examination of musculoskeletal system of mice by means of fluorescent microscopy revealed that the ligation of the common bile duct caused a deposition of pigment in the articular cartilages, intervertebral disc, epiphyseal plates and pulp of the teeth.¹ These experimental studies suggested that some of the pigment permeates into the articular cartilage from the surrounding synovial fluid and that there is a free exchange of tissue fluids in the intervertebral disc.

TREATMENT

Although the administration of vitamin C was suggested and has been tried for alkaptonuria and ochronosis, no definite improvement has been reported.² As for surgical treatment this should be limited only to relieve fixed locking in the knee or any other large joint when caused by free bodies. In instances of severe osteoarthritis of the knee or hip arthrodesis procedures are indicated.

CONCLUSION

The entity of alkaptonuria and ochronosis can be recognized by the presence of pigmentation of the nose, ears, sclera and skin by the detection of alkapton bodies in the urine and by radiographic evidence of premature osteoarthritis of large joints and calcification of the intervertebral disc tissues. In the differential diagnosis of osteoarthritis especially with the presence of free intra articular bodies as noted on radiographic examination consideration should be given to alkaptonuria as a possible etiologic basis. A case illustrating some of these findings has been presented.

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Of the 183 per cent patient mortality, 125 per cent consisted of diabetic patients and 58 per cent of nondiabetic. The mortality for staff patients was 125 per cent, compared to 58 per cent for private patients. The average hospital stay for minor amputations was 31.3 days for major amputations 39.2 days and for combined major and minor amputations 39.6 days (Table IV).

TABLE IV ANALYSIS OF HOSPITAL STAY, PRE AND POSTOPERATIVE DAYS

	DIABETIC				NONDIABETIC				AVERAGE	
	STAFF		PRIVATE		STAFF		PRIVATE			
	PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST
Minor	7.9	19.4	5.4	15	8	4.4	17	8.5	9.6	21.7
Major	11.2	30.4	8.8	33	11.5	37.6	10.4	13.8	10.5	28.7
Minor and Major	9.4	47.7	8	32.3	4.5	21	0	0	7.3	32.3
Average	9.5	31.2	7.4	26.8	8	31.2	13.7	11.2		

COMMENT

The fact that 52.6 per cent of the patients who had toe amputations were subjected to a thigh amputation within three months seems at first glance to indicate poor surgical judgment. Table VI shows that the operative mortality

TABLE V CAUSE OF DEATH IN NINETEEN PATIENTS

NUMBER OF DEATHS	CAUSE
Coronary thrombosis	2
Cerebral thrombosis	1
Cerebral thrombosis or hemorrhage	1
Mesenteric thrombosis	1
Uremia (†) nephrosclerosis	1
Progressive ischemic necrosis of leg	1
Progressive ischemic necrosis of stump	1
Pneumonia	4
Bronchiectasis	1
Pulmonary infarction	1
Stump infection	1
Welch Bacillus infection	2
Acute pyelonephritis	1
Failure of recovery from anesthesia	1

TABLE VI ANALYSIS OF GROUP OPERATIVE MORTALITY

	NUMBER OF OPERATIONS	DEATHS	PER CENT
Minor	76	3	3.9
Major alone	59	9	15.5
Major preceded by minor	30	7	23.3

for the group of patients having combined operations is decidedly higher than the mortality for the group having only a thigh amputation (23.3 per cent to 15.5 per cent). Sixteen of the thirty patients having combined operations were staff patients with diabetes who were admitted to the hospital with acidosis and a marked state of dehydration. In many instances there was superimposed infection. In a few cases permission for a primary thigh amputation was not granted by the patient or the family.

The successful toe amputations were performed only when necrosis was limited to the toe itself when infection was minimal, and when there was some

TABLE I GENERAL STATISTICS

Number of patients	104
Male 61 Average age, 63.4 years	
Female 40 Average age 69.9 years	
Patients with minor amputations	27
Patients with major amputations	47
Patients with minor amputations followed by major within 3 mo	30
Number of amputations	164
Major, 58	
Minor, 46	
Major and minor combined, 60	
Average time interval between minor and major amputations (combined)	23.4 days
Mortality	
Minor, 2.9%	
Major, 13.4%	
Total mortality (based on number of patients)	18.3%

instances the distal end of the corresponding metatarsal bone. The anesthetic agents, ether, cyclopropane, intravenous sodium pentothal spinal block and refrigeration, varied so much that no group was large enough to be analyzed statistically. The patients were divided into staff and private as well as diabetic and nondiabetic. I believe there is no fundamental difference in the arteriosclerotic lesions in diabetic and nondiabetic patients.¹² The altered metabolism in the diabetic patient, however, increases the operative risk and these patients should be analyzed separately.

TABLE II ANALYSIS OF 104 PATIENTS WITH AMPUTATIONS FOR ARTERIOSCLEROSIS OBLITERANS

	DIABETIC		NONDIABETIC		TOTAL
	STAFF	PRIVATE	STAFF	PRIVATE	
Minor	15	8	2	2	27
Major	10	10	11	10	41
Minor and major	16	7	7	0	30
Total	41	25	20	18	104

In 104 patients (Table I) there were 164 amputations of which eighty eight were major and seventy six minor. Sixty six of the patients were diabetic and thirty eight were not (Table II). Sixty-one of the patients were cared for by the resident staff and forty three had private attending surgeons. Of the fifty seven patients who underwent toe amputations thirty, or 52.6 per cent, were followed within a three month period by a thigh amputation. Twenty three of these thirty patients were staff and seven private. Twenty three were diabetic and seven nondiabetic. Nineteen of the 104 patients died giving a patient mortality of 18.3 per cent and an operative mortality of 11.6 per cent.

TABLE III ANALYSIS OF 164 MINOR AND MAJOR AMPUTATIONS

	DIABETIC				NONDIABETIC				TOTAL	
	STAFF		PRIVATE		STAFF		PRIVATE			
	NO	%	NO	%	NO	%	NO	%	NO	%
Minor	28	17.1	14	8.5	2	1.3	2	1.3	46	28.2
Major	10	9.1	11	6.7	14	8.5	18	11	58	35.3
Minor and major	38	19.5	25	8.5	16	9.5	20	12.3	60	36.5
Total	75	45.7	39	23.7	30	18.3	40	12.3	104	

A SIMPLE PROCEDURE FOR THE CONTROLLED ADMINISTRATION OF INTRAVENOUS FLUIDS

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THE administration of intravenous fluids for the treatment of shock is undertaken usually with inadequate knowledge of the patient's circulating blood volume. During a recent study,¹ it became clear that simple methods for the determination of mean arterial pressure and of plasma volume would be desirable both as a guide to choice of therapy and as a means of assessing the therapeutic response. Hitherto, the equipment needed for this determination has been too cumbersome for use in the average hospital emergency or surgical ward. In the present study, a simple procedure was devised for the determination of plasma volume by means of a small visual comparator² and for the measurement of intra arterial pressure by means of the Tyco's aneroid manometer. Further, a kit has been designed to include in compact form all equipment needed for the administration of intravenous fluids, the measurement of mean arterial pressure, and the determination of plasma volume.

The salient features of the technique include the insertion of a small indwelling catheter into a medium sized vein of the forearm and the insertion of a Lindeman type needle into the femoral or brachial artery. The indwelling venous catheter permits of dye injection for plasma volume determination and allows for repeated administration of intravenous fluids over a considerable period of time. The indwelling arterial needle establishes a convenient and reliable route by which blood samples for plasma volume determination and other laboratory tests may be obtained as well as providing a means of measuring mean arterial pressures.

DESCRIPTION OF THE KIT

The kit* illustrated in Fig 1 consists of a wooden cabinet 18 inches long, 12 inches high, and 8 inches wide, the interior of which has been so designed as to permit ready access to almost every article. The list of contents and their disposition in the kit is given in Fig 1.

Three of the instruments in the kit require further description. The first of these is the anesthetic syringe†. This is constructed of metal and is in fact no more than a metal frame with a piston. When loaded with the metal cap

*The work described in this paper was done under contracts recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Columbia University. Additional support was provided by the Commonwealth Fund.

anestube' it is used like the ordinary syringe. The anestube syringe has been included in the kit because together with the T 1824 anestubes* it offers the most practical means of injecting an exact amount of T 1824 with minimal loss. Each anestube contains exactly 15 mg of the blue dye T 1824 in 5 cc of normal saline solution. These tubes are made to deliver their contents within plus or minus 0.03 per cent but since aspiration is a feature of this syringe the anestubes may be washed two or three times to insure delivery of all the dye. Such a system avoids using a specially calibrated glass syringe which must be filled from a separate ampule of dye—a less accurate and more time consuming procedure.

The visual comparator† for plasma volume determination has been designed to measure the color of a single sample taken ten minutes after the intravenous injection of dye. The validity of this single measurement has been established by Noble and Gregersen‡. Two color disks are supplied with the comparator. Disk A is made up of ten colored glass standards which cover a range of total plasma volumes between 1200 and 3200 cc. Disk B covers a range between 2300 and 6800 cc. Each glass standard was made to match the color of a 10 mm depth of a liquid standard of known dilution. The total plasma volume corresponding to each glass standard was calculated on the basis of a 15 mg injection of T 1824. In the event therefore that more or less than 15 mg of dye are injected the true volume must be computed as follows:

$$\text{Disk reading} \times \frac{\text{mg of dye injected}}{15} = \text{True volume}$$

The reliability of this method for the determination of total plasma volume depends largely upon obtaining absolutely clear serum samples. This may be achieved readily if each blood sample is delivered into an oil coated test tube. By this means hemolysis is prevented. It is advisable although not essential to have each patient fast at least eight hours before study to avoid lipemia. If the sera are clear color matching is not difficult. However as in all colorimetric methods individual judgment plays a major role. Some practice is necessary before discrimination between color differences in the high ranges is achieved. Results obtained with the comparator indicate that it measures plasma volume differences in excess of 5 per cent.

A simple method for the measurement of mean arterial pressure using the Tyco aneroid manometer has been devised. A 10 cm length of rubber tubing partially filled with citrate is attached to the manometer. The free end fitted with an adapter is attached to the shrink of the arterial needle. The mean pressure recorded by the aneroid needle is read directly from the face of the manometer. It requires less than a minute to make a single determination.

PREPARATION OF THE PATIENT

1. For the purpose of dye injection and the intravenous administration of fluids a specially designed plastic venous catheter† is used. This is kept

*Supplied by the Research Department of the Novocel Chemical Mfg Co. Brooklyn, N. Y.
 †Supplied by the Heli-ge Inc., Long Island City, N. Y.
 ‡Supplied by the U. S. Catheter Company, Glens Falls, N. Y.

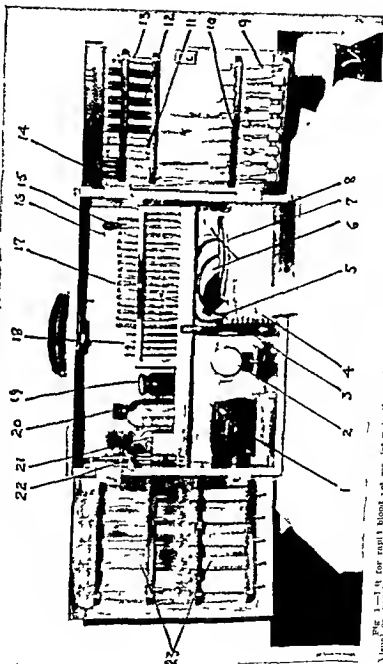


Fig. 1.—A diagram of a blood separator and transfusion machine. The diagram shows a cross-section of the machine. The main components are labeled as follows: 1. The base of the machine. 2. The motor or pump. 3. The drive shaft. 4. The drive pulley. 5. The drive belt. 6. The drive pulley. 7. The drive belt. 8. The drive pulley. 9. The main cylindrical component. 10. The internal structure of the main component. 11. The internal structure of the main component. 12. The internal structure of the main component. 13. The internal structure of the main component. 14. The frame of the machine. 15. The frame of the machine. 16. The frame of the machine. 17. The handle of the machine. 18. The main shaft of the machine. 19. The main shaft of the machine. 20. The main shaft of the machine. 21. The main shaft of the machine. 22. The main shaft of the machine. 23. The main shaft of the machine.

finger at an angle of about 45 degrees. As progress is made in the direction of the pulsating vessel, the thumb is removed from the patent stylet at intervals to ascertain whether or not the artery has been punctured. When puncture of the artery has been accomplished, blood will be seen to drip from the patent end of the stylet. The flange of the needle is then grasped with one hand, the patent stylet with the other. Coincident with the slow removal of the patent stylet, the arterial needle is "threaded" into the lumen of the vessel. When the stylet has been removed, blood should spurt from the end of the needle. The solid stylet is then placed in the needle and stylet and needle together are threaded further into the vessel in order that a substantial portion of the needle shall lie within the lumen of the artery. It is advisable at this juncture to make sure that there is a free flow of blood from the needle by removing the stylet for a moment. As a precaution against clotting in the needle, the solid stylet should be dipped into the bottle of hydrogen peroxide before it is replaced. (During blood sampling, the stylet should stand in the peroxide.) As soon as the needle is in place it should be taped securely to the thigh. Should the patient be under anesthesia or unable to lie quietly in bed, the leg should be immobilized by means of a restraint over the knee.

PLAN OF STUDY

The procedure recommended for the study and follow up of a patient requiring controlled fluid therapy will be described under three headings: the pretherapeutic period, the period of therapy, and the post therapeutic period.

Pretherapeutic Period—During the first period, a single determination of plasma volume is made. This requires the withdrawal of a preinjection arterial sample, the intravenous injection of dye, and the withdrawal of a post injection arterial sample exactly ten minutes later. In addition measurements of pulse, respiratory rate, and mean arterial pressure are repeated two or three times. Should blood be required for hematocrit or serum protein determinations this should be taken either before the injection of dye or after the withdrawal of the ten minute arterial sample.

Period of Therapy—Intravenous fluid is administered through the three way stopcock and catheter. When the infusion or transfusion is completed the saline drip is again started at the usual slow rate (6 drops per minute), or the plastic stylet is threaded into the venous catheter.

Post Therapeutic Period—All the measurements made during the pretherapeutic period are repeated shortly after transfusion or infusion and again a few hours later. The results will show the response of the patient to therapy and will serve as a guide to further management. Should there be gradual blood loss as is sometimes encountered in a postoperative patient, this will be reflected in the measurements obtained. Although a fourth study can be undertaken six or seven hours after therapy, if necessary, it is not recommended because a fourth injection of blue dye may give a bluish tinge to the skin and mucous membranes. Although this is not harmful, it may be upsetting to the patient.

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MEASUREMENT OF MEAN ARTERIAL PRESSURE

A 10 cm length of gum rubber tubing with adapter secured at one end is held in the shape of a U by the left hand. A 5 cc syringe is filled with sodium citrate solution and used (without needle attached) to deliver approximately 2 cc of the solution into the free end of the tubing. This quantity will fill the tubing approximately to the halfway point. While the tubing is still held by the left hand in the U shaped position, the aneroid manometer is fitted into the free end of the tubing with the right hand. Once attached, the tubing may be allowed to hang freely from the manometer without fear of losing citrate solution. The manometer and tubing are now ready for use and should be placed upon the bed close to the arterial needle. With the left hand used to steady the arterial needle the right hand removes the solid stylet. At the moment of removal, the thumb of the left hand is placed over the shank of the needle to stop the flow of blood while the stylet is placed in the beaker of peroxide. The adapter on the end of the aneroid tubing is then fitted into the shank of the arterial needle and the aneroid held in the upright position just above the level of the needle. If the oscillation of the aneroid needle is sluggish and the pressure mounts continuously the system is not patent. The manometer and tubing should be detached, the tubing flushed with citrate and refilled. To insure patency of the needle the stylet should be placed within the needle for a moment. The mean arterial pressure is taken as the average of the highest and lowest swing of the aneroid needle. This oscillation usually covers a range of from 2 to 4 mm.

DETERMINATION OF PLASMA VOLUME

Approximately 2 cc of heparin mineral oil are delivered into each of four centrifuge tubes. Next the amputube syringe with Luer Lok adapter attached is loaded with the dye cartridge, the cartridge locked in and the piston screwed into the rubber plunger.

1 *Withdrawal of Dye free sample*—A clean 10 cc syringe with adapter attached is used to collect the dye free arterial sample. After withdrawal of the stylet the syringe is fitted into the shank of the arterial needle and about 13 cc of blood are taken (more if hemocoagulation is present). Delivery of the blood into the oil coated test tube requires a little practice. First the adapter is removed from the end of the syringe. The syringe is grasped in the right hand while the test tube is held in the left hand in a horizontal position and rotated slowly so that the entire inner surface of the tube becomes coated with oil. The horizontal position of the tube is maintained and the rotary motion continued while the tip of the syringe is placed against the inside surface of the test tube and about 5 cc of blood are delivered slowly. As the test tube is being filled the tube and syringe are gradually brought into the upright position so that no spilling occurs. This tube is then replaced in the rack and a second tube coated with oil and filled in the same way from the same syringe. The purpose of the oil coated test tube is to prevent hemolysis.

Experience has shown however that the oil coated test tube is not indispensable that if the blood is delivered slowly into a clean test tube without oil a clear serum sample can often be obtained. It may be time saving, therefore to take one sample without oil. A small amount of blood is held within the syringe for an hematocrit determination*. A few grams of purified heparin are placed in one of the Wintrobe tubes a No. 19 gauge needle is attached to the syringe and the remainder of the blood is delivered into the tube by placing the full length of the needle in the tube and giving a forceful thrust upon the plunger. In this way the tube may be filled to the top without trapping any air in its lumen. The tube is then placed in the rack and the blood stirred gently with a thin piece of wire. The time at which these samples are withdrawn is noted on the protocol sheet.

2 *Injection of Dye*—The injection of dye should be undertaken with care so that none is lost. The tip of the anesthetic syringe (already loaded with the appropriate dye cartridge) is screwed snugly into the open arm of the three way stopcock. The handle of the stopcock is then turned to permit direct injection of dye into vein and the dye injected. Accurate note is made of the time of this injection. Once the syringe has been emptied of dye it is washed three times with saline solution from the infusion ampule. By manipulating the stopcock handle saline solution is first aspirated into the syringe and then injected into the vein. In this way all of the dye is delivered into the circulation.

3 *Withdrawal of Ten minute Sample*—Ten minutes after the injection of the dye another 13 cc of arterial blood are withdrawn from the femoral artery in the manner described and the blood is divided between two sampling tubes and a Wintrobe hematocrit tube.

4 *Centrifugation*—The duplicate dye free serum and dye serum samples require ten minutes of centrifugation at approximately 2000 r.p.m. This may be accomplished with a small angle centrifuge or if need be a hand centrifuge. After centrifugation a clear layer of serum will be found to lie between the packed red blood cells and the oil. Should there be a fibrin clot in the serum a small glass spatula is used to push it gently downward. In this case centrifugation usually has to be repeated.

5 *Transfer of Serum*—With two clean capillary pipettes the dye free and the dye samples are transferred into each of two square test tubes as follows: before introduction of the pipette into the oil most of the air is expelled from the pipette. As the tip of the pipette is advanced through the oil a few air bubbles are expelled from the pipette in order to prevent the entrance of oil into it. The tip is then advanced into the serum and the serum aspirated. In removing the filled pipette care should be taken not to aspirate the oil. This may be prevented by maintaining slight pressure on the rubber bulb. The end of the pipette is then wiped with a piece of gauze and the sample delivered into the square test tube.

*This may be obtained by the copper sulfate method.

ABSORBABLE FIBRIN TUBES FOR VEIN ANASTOMOSES

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IT WAS not until the advent of aseptic surgery that substantial progress was made in the field of vascular anastomoses. The most successful methods of restoring continuity in blood vessels may be divided into two general groups (1) by careful direct suture and (2) by the use of mechanical devices.

The fundamentals of the suture method established by such workers as Jassinowsky,¹¹ Jensen¹² and Carrel¹³ entail the use of very small needles and fine suture. In spite of the greatest care thrombosis is a common cause of failure to produce a satisfactory anastomosis. The operating time required to complete such meticulous anastomoses by direct suture and the disappointing results which frequently follow them led several experimenters to develop methods whereby mechanical devices could be used for uniting vessels more quickly and more successfully.

At the International Medical Congress of 1897 Nitze¹⁴ demonstrated the use of a small ivory ring. This was threaded over one end of a divided vein which was then turned back over the ring so that the intima was exposed and was secured by a circumferential ligature. The vein covered ring was then inserted into the other end of the vessel and all these structures were held in place by a mechanical device not clearly described.

A magnesium prosthesis similar in principle to Nitze's ivory ring was described by Payr¹⁵ in 1904. In the same manner one end of a severed vessel was threaded through the metallic ring, turned back over the ring and anchored with a circumferential ligature. This was inserted into the other end of the divided vessel and a second ligature held both parts of the artery (or vein) securely on the ring. Thus the magnesium ring acted as a supporting structure and allowed the two vessel segments to be approximated intima to intima. This method was not uniformly successful. Magnesium in the process of absorption becomes a highly basic salt and provokes violent tissue reaction¹⁶ which may account for some of the poor results obtained. Payr minimized the distortion which was brought about by the gas filled cysts and the extensive fibrosis produced by the magnesium disintegration.

Blakemore, Lord and Steffen¹⁷ have devised a highly successful "non-suture method" of vessel anastomosis using rigid tubes made of vitallium—a material which excites little tissue response. The concept of using a vitallium tube lined with a vein graft to bridge an arterial defect is a unique contribution to military and traumatic surgery. Another field of usefulness for the Blake

more technique is concerned with the establishment of venous shunts in patients with portal hypertension. In adults, the use of a vitallium tube has provided a satisfactory method for making such anastomoses. In contrast, this method of inserting a nonabsorbable tube has certain limitations when used in children because the vein lumen (at the anastomosis) cannot possibly increase in size during the subsequent growth of the patient.

This indicated limitation of the Blakemore tubes in children has prompted us to search for a material which (1) would be rigid, (2) would cause little reaction in animal or human tissues and (3) would be absorbed by the host in a matter of several weeks or months. Such a substance would permit manufacture of tubes for performance of nonsuture methods of vascular anastomoses. If an appropriate material could be found and employed for vascular anastomoses in children, the subsequent absorption of the rigid tube would allow the vein (or artery) to expand and grow as the individual becomes older.

We were particularly attracted to the possibilities of fibrin film (prepared from human plasma by the methods of Ferry, Morrison and associates¹⁰) since this material has already been studied by Ingraham and his associates,¹¹ who were interested in using it as a dural substitute. They tested fibrin film and found that it gave a minimum of tissue reaction (in monkeys and human beings) and was completely absorbed in six to eight weeks.

The present investigation is concerned with observations made during and after vascular anastomoses using plasticized, fibrin cuffs to aid in vein reconstruction with a nonsuture technique. The fibrin was prepared by the blood fractionation laboratory of the department of physical chemistry at Harvard Medical School.*

Fibrin film is made from fibrin plasticized by water and pressed into a thin sheet. Strips of this material 2 or 3 cm. wide were rolled around a glass rod of the desired diameter until the wall of the tube was 0.5 or 1.0 mm. in thickness. The seamless tube thus produced was left on its glass rod and placed in a test tube for steam sterilization. After sterilization the fibrin cuff was slipped off the rod (under sterile conditions) and was placed in a stoppered sterile tube. It could be kept in this state indefinitely until it was used.

About ten minutes before a fibrin tube is to be used it must be placed in normal saline solution. This changes the firm leathery consistency of the dried film to a more pliable texture the surface of which may be indented. In spite of this pliable quality of the tubing a circumferential ligature may be tied around it with only a minimal diminution of its internal diameter. As the fibrin tube absorbs fluids from the tissue in which it is implanted, it swells slightly, causing the circumferential ligature to become tighter and less likely to slip.

EXPERIMENTAL OBSERVATIONS

Dogs were used in all the experiments. The abdominal vena cava or a jugular vein was employed for the various anastomoses (Figs 1 to 6). Twenty

*Under the direction of Dr. Edwin Cohn. For the actual formation of the seamless tubes of fibrin film we are indebted to Dr. John D. Ferry and Peter H. Morrison.

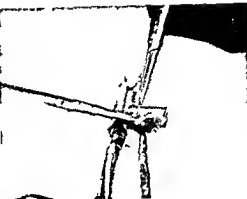
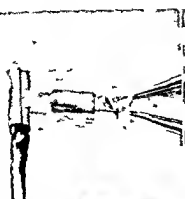


Fig. 1

Fig. 2

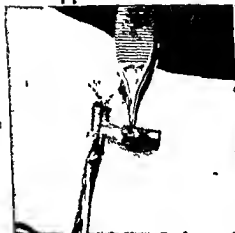


Fig. 3

Fig. 4



Fig. 5

Fig. 6

Fig. 1—Exposing nonsuture anastomosis of vein. Fibrin film tube has been threaded on to proximal segment of vessel which is compressed by rubber-covered clamp.

Fig. 2—Vein has been turned back over fibrin tube by traction on three hemostats placed at equidistant points on cut end of the vein.

Fig. 3—Turned back vein held on fibrin tube by a fine chronc catgut circumferential suture.

Fig. 4—Distal segment of vein has been pulled on to the fibrin tube and the turned back over it.

Fig. 5—Anastomosis completed by securing the distal end of vein over fibrin tube with second chronc catgut circumferential suture.

Fig. 6—Occluding clamps have been removed and blood is passing through the anastomosis.

seven anastomoses were carried out.* A rigid aseptic technique was used. Skin preparation consisted of mechanical scrubbing using alternate sponges of zephiran and alcohol.



Fig. —Vein exposed eight weeks after anastomosis. Lumen is patent. There is no thrombosis or narrowing of lumen.

The jugular vein or vena cava was exposed for a distance of about 5 cm and the vessel was occluded with rubber covered clamps gently applied. The vessel was then divided midway between the clamps and a fibrin cuff from 5 to 8 mm in length was threaded onto the proximal segment. The end of the vein was then grasped with three fine pointed hemostats and then turned back.

TABLE I SUMMARY OF DATA

ANIMAL NO	VEIN EMPLOYED	ANIMAL SACRIFICED AFTER (NUMBER OF WEEKS)	FIBRIN CUFF REMAINED	
W 8	Jugular	4	None	
115 40	Jugular	8	None	
100 45	Jugular	7	None	Good
100 40	Right jugular	4	Yes	Fair no thrombus
103 45	Left jugular	7	None	Good no thrombus no constriction
	Right jugular	7	None	Good no thrombus no constriction
100 40	Left jugular	3	Yes	Good no thrombus
	Right jugular	3	Yes	Good no thrombus
106 40	Left jugular	8	None	Good no thrombus no constriction
	Right jugular	8	None	Good no thrombus no constriction
12 40	Left jugular	18	None	Good no thrombus 20% constriction
	Right jugular	18	None	Good no thrombus 20% constriction
108 45	Left jugular	7	None	Good no thrombus slight constriction
	Right jugular	7	None	Good no thrombus slight constriction
109 40	Left jugular	6	None	Good no thrombus no constriction
	Right jugular	6	None	Good no thrombus no constriction
130 40	Vena cava	8	None	Good no thrombus 30% constriction
130 40	Vena cava	16	None	Good no thrombus 30% constriction
134 40	Vena cava	10	Yes	Good no thrombus
125 40	Vena cava	9	Yes	Good no thrombus
136 45	Vena cava	12	None	Good no thrombus 30% constriction
137 40	Vena cava	16	None	Lumen obliterated by regaining fibrosis
138 40	Vena cava	2	Yes	Good no thrombus
140 45	Left jugular	4	None	Good no thrombus
	Right jugular	4	None	Good no thrombus
141 45	Vena cava	3	Yes	Good no thrombus
144 40	Right jugular	7	None	Good no thrombus slight constriction

*Following completion of the present work, similar anastomoses were made on arteries with satisfactory results.

over the fibrin cuff. A ligature of 0000 chromic catgut was tied over the turned back vein to hold it onto the cuff. Over this preparation the distal end of vein was then drawn (by three fine hemostats which grasped its end). A second circumferential ligature of 0000 chromic catgut was tied over this juncture securely uniting the two portions of the vessel. The rubber shod clamps were then removed. In no instance was there bleeding after the clamps were taken off. All wounds were closed with interrupted black silk sutures. The animals were kept for periods varying from two weeks to four and one half months after operation.



FIG 8—Two specimens of veins removed eight weeks after nonsuture method of anastomosis employing an absorbable fibrin tube. The intima is smooth and there is no intraluminal clot.

The selection of a fibrin tube of proper size is imperative for the success of an anastomosis. The cuff must be of such diameter that the vein can be easily turned back upon it since stretching the structure over a tube of too great size will produce tears which invite thrombosis. Large dogs weighing thirty to fifty pounds were used for the jugular vein anastomoses. In these animals a fibrin tube 6 to 8 mm. in length with an inside diameter of $\frac{1}{4}$ to 5 mm. could be used.

RESULTS OF EXPERIMENTS

In Table I is given detailed information regarding the individual experiments. The condition of the anastomosed vein was studied in each case at a subsequent date by sacrifice of the dog, removing the vessel and making a careful gross and microscopic examination of the specimen. Thrombosis had not occurred in any instance. When opened, the vessel intima was smooth and glistening (Fig. 8) and the precise line of anastomosis was often difficult to identify. In twenty six specimens the vessel had a lumen of satisfactory size. In several specimens there was a slight constriction of the vessel at the anas-

TABLE II TIME OF DISINTEGRATION AND ABSORPTION OF FIBRIN CUFFS AS FOUND IN AUTOPSY EXAMINATIONS

	1 WK.	2 WK.	3 WK.	4 WK.	5 WK.	6 WK.	7 WK.	8 WK.	10 WK.	11 WK.	12-18 WK.
Dogs with fibrin cuff remaining	1	3	1	2					1		
Dogs with fibrin cuff disappearance						0	4			1	4

tomatic site. In one vena cava experiment the vessel had become obliterated by fibrosis resulting from extensive regional infection.

The time necessary for the absorption of the fibrin cuff is of considerable interest. The data are summarized in Table II. In dogs sacrificed before six weeks three had no fibrin remaining and six had some of the cuff still in place. In animals kept more than six weeks only one had some film remaining. In short the fibrin cuffs usually disappeared in six or seven weeks (Fig 9).



FIG 9.—Photograph of vein anastomosis 4-6 weeks after operation. The fibrin tube has disappeared.

CONCLUSIONS

Description is made of a nonsuture method of vascular anastomosis wherein the vessel segments are brought together over a fibrin cuff making an intimal lined reconstruction. The fibrin tubes disappear usually in six or seven weeks. This leaves an anastomosis which is adequate in size which is not constricted by a metallic ring (as in the Blakemore method) and which can enlarge in diameter with any subsequent growth of the individual.

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A SELF RETAINING RETRACTOR FOR HEMI-LAMINECTOMY

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IN THE past few years several retractors have been designed for the purpose of giving adequate exposure in operations upon the spinal canal, and for the purpose of unilateral approach. In my experience they have failed to meet one or more of the following desirable features: adequate exposure, minimum interference in the operative field, absence of tendency to rotate when the blades are



Fig. 1—Showing the upright arms of the blades hinged so that they may be folded over and out of the operative field.

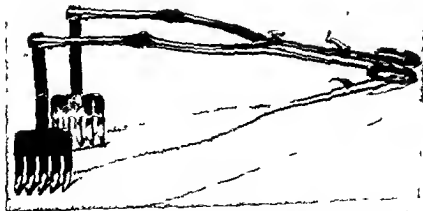


Fig. 2—Showing that the blades of the retractor are adjustable to any required depth.

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set at different levels, and sufficient fixation of the blades in the soft tissues to keep the instrument from jumping out of the wound when force is applied. The retractor presented was designed with these requirements in mind and, in my experience, it has successfully fulfilled these requirements.

This retractor is a modification of other cerebellar self retaining retractors. The upright arms of the blades are so hinged that they may be folded over and out of the operative field (Fig 1), thus giving adequate exposure without interfering with the operator's approach. The tendency of a retractor to jump out of the wound when adequate retraction of the muscles is obtained has been overcome by the sufficiently sharp curve of the blades of this instrument. Adequate fixation of the opposing blade against the spinous process is also provided. In addition to its function as a hemilaminectomy retractor, this instrument gives satisfactory bilateral exposure in any region of the spine desired. The blades of this retractor are adjustable to any required depth and are always at a right angle to the operative field (Fig 2).

The blades of the retractor are 4 cm in length, 3.8 cm in width, and 0.5 cm in thickness at the thickest part. The upright extensions of the blades are 6 cm long and are hinged at 2.4 cm from the shoulder of the blade itself. The angle of the blades varies from 0 to 52 degrees. The limbs of the retractor are also hinged at a distance of 6.5 cm from the center of the slots which hold the upright extensions of the blades. The instrument was made by V. Mueller Co. of Chicago, according to my design.

VASCULAR SYSTEM OF THE LONG BONES OF THE RAT

SAMUEL M. REICHEL, M.D.,* ROCHESTER, MINN.

IN RECENT years there has been a considerable increase of interest in the supply and circulation of blood in the bones.^{1, 2} Various methods have been employed to overcome the many difficulties encountered in studying the circulation within such an intractable structure as bone. Among these have been the injection of radiopaque substances,³ suspensions of fine carbon particles,^{4, 5} vital stains,⁶ the study of serial sections,⁷ and procedures in which part of the circulation to the bone is interrupted in the living animal.⁸

The present study is based on an adaptation to bone of the neoprene injection corrosion technique which has been employed so successfully in vascular research on soft tissue. The injection material was a neoprene suspension supplied by the manufacturer in several colors, black and white having been employed in this work for best contrast. As received, the suspension was too thick for injection of capillaries and small arterioles, and therefore 40 parts of distilled water were added to 60 parts of neoprene suspension in the routine procedures. This material, when injected into blood vessels, coagulates spontaneously or when exposed to acids, alcohol, formalin and many other substances, producing an elastic cast which conforms closely to the contours of the vessels. Such specimens have been preserved in alcohol (90 per cent) and in water for as long as two and one half years and at the end of that time the neoprene casts were still elastic and strong.

Albino rats of both sexes and of weights ranging from 150 to 400 Gm. were employed in this work. In the rat the epiphyses are retained throughout life and do not fuse to the metaphyses at maturity as is the case in man. The bones studied were the tibia and femur. The animals were killed by bleeding under pentobarbital sodium anesthesia. The injections were made immediately into the abdominal aorta and the inferior vena cava. Prior to injection of the neoprene suspension isotonic saline solution was perfused through the aorta until the perfusate returned grossly clear. The cannulae used were made of glass and their tips were carefully ground and beveled. The perfusate and neoprene suspension were warmed before injection to approximately 90° F. Mercury manometers revealed the injection pressures at all times during the injection. Arterial injections were made at 200 to 300 mm. of mercury, venous injections at 20 to 100 mm. of mercury. By means of a rubber bulb in the system pulsations could be imparted to the injection fluid by the operator.

Following injection the two specimens were skinned and removed from the animal and placed in 90 per cent alcohol or in 10 per cent solution of formalin until studied. In a number of the specimens the vessels were dissected

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down through the soft tissues and traced to the bone. In others the bones were denuded and embedded horizontally in paraffin for one half of their circumference. Then the exposed portion of the bone was corroded with concentrated hydrochloric acid or 25 per cent solution of sodium hydroxide or potassium hydroxide. Thus the injected vessels could be examined and studied in relation to the remaining bone. When the vascular relations had been studied, denuded bones were dropped into concentrated hydrochloric acid and the neoprene casts which remained after corrosion were complete were studied. Most of the specimens were studied in this manner (Fig. 1). Other specimens were placed in methyl salicylate which is capable of clearing cortical bone and cartilage of

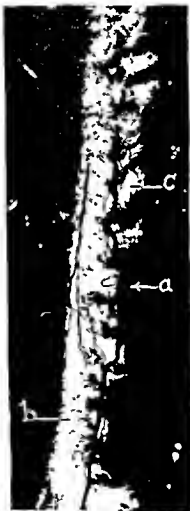


Fig. 1. System of bone marrow of rat showing vascular system of main nutrient arterial system. b long freely anastomosing venous capillary sinuses. c capillary sinuses have been injected in this specimen.

rats to a fair depth so that vessels could be visibly traced into the bone with ease and with certainty. Other specimens were imbedded in lucite, although this method of treatment had no advantages over other methods. Some specimens were decalcified and the vessels were dissected as they passed through the softened bone. In other specimens the cortical bone was removed locally by drilling, under water, with fine dental burs.

GENERAL CONSIDERATION

Ordinarily the higher the injection pressure the more complete was the injection of the specimen. With fairly high injection pressures however, some of the vessels within the bone marrow ruptured and formed artefacts of two types. Where a vessel ruptured in the region of the endosteum there would be a dissection of the marrow from the bone by the extravasated injection fluid, a thin sheetlike artefact being produced. Where small arteries or arterioles were ruptured within the marrow substance proper a rounded cotton ball like artefact was produced with the artery approximately in the center of the mass. By treating these artefacts with xylol the rubber was softened and could be dissected down to the actual break in the vascular continuity. Artefacts were less common when the arteries and veins were injected simultaneously than when a single system was injected. When present the artefacts were found most often in the metaphyseal regions.

Because of the long narrow shape of the tibia and femur the study of the neoprene casts of the marrow vessels was rather difficult. Examination had to be performed under water to minimize tangling of the elongated delicate branches of the nutrient artery. Even under the best conditions arterial capillaries often became entangled so that one could not be sure whether one was observing an anastomosis or an artefact. For this reason no statement can be made in regard to the occurrence of capillary arterial anastomoses.

Although the neoprene corrosion method was found to be an excellent means of studying the bones of rats it is not believed that the efficiency of the circulation within a given bone can be gauged accurately by a study of the neoprene vascular casts produced by injection. There are too many variables involved and only a very rough approximation could be reached.

Regarding the importance of the nutrient vessels the literature contains a number of studies.^{4,5,6} The present study has indicated that while the nutrient vascular system was well developed and profuse there were other less conspicuous circulatory channels which were probably just as important as the nutrient vessels. Such arteries were small and individually capable of contributing only a modest increment to the blood supply of the bone. However they were numerous and collectively could be considered an important source of blood. In the bones studied they were found to be most abundant in the distal half of the femur and the proximal half of the tibia (Fig. 2). None were found in the distal half of the tibial shaft. In their course along the surface of the bones the vessels rested in grooves similar to that of the main nutrient artery. They almost always entered the cortex in the same

direction as the main nutrient artery (proximally in the femur, distally in the tibia). After piercing the outer layer of cortex the vessels took a direct course to the marrow cavity. These arteries were traced into the marrow. For reasons mentioned previously it cannot be said, at this time, whether or not the vessels anastomosed with terminal branches of the main nutrient artery. Because of their characteristics they may be considered minor nutrient arteries.

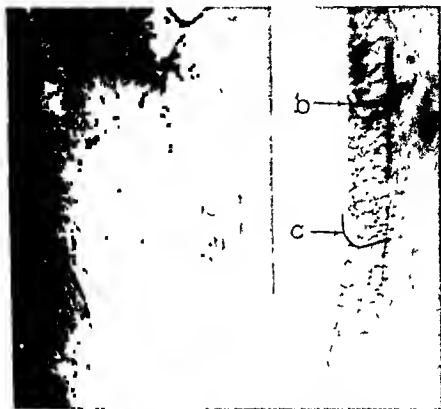


Fig 2—*a* Minor nutrient arteries entering anteromedial aspect of proximal tibia. *b* and *c* Minor nutrient arteries passing through cortex of femur. Longitudinal section of decalcified femur viewed on edge. In *b* bifurcation is demonstrated midway through cortex (*a* $\times 14$, *b* and *c* $\times 20$).

The injection material used in this study demonstrated beautifully the profuse lacy network of periosteal vessels. These vessels could be traced easily into the Haversian system. The Haversian canals themselves received the injection medium only when high pressures were employed. Neoprene injection offers no particular advantage over other methods of study, in so far as Haversian vessels are concerned.

GROSS BLOOD SUPPLY OF FEMUR

The neoprene vascular casts revealed a surprisingly rich network of blood vessels in the femoral marrow cavity. The main nutrient artery entered the

rats to a fair depth so that vessels could be visibly traced into the bone with ease and with certainty. Other specimens were imbedded in lucite, although this method of treatment had no advantages over other methods. Some specimens were decalcified and the vessels were dissected as they passed through the softened bone. In other specimens the cortical bone was removed locally by drilling, under water, with fine dental burrs.

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physal regions, although some branches supplied capillaries to the central marrow and others to the peripheral marrow and the adjacent Haversian systems

In addition to the main nutrient arterial system, the marrow cavity was also supplied by the minor nutrient arteries. These vessels were best demonstrated in the tibia and will be described later

The nutrient vein, which accompanied the artery through the nutrient foramen was a well developed structure. Traced into the marrow cavity, it was seen to originate from the central sinus, a wide capacious channel extending the length of the marrow cavity and studded with innumerable branches of various sizes. Some of the branches, the communicating sinuses, were large and formed nearly a right angle with the central sinus. The communicating sinuses were most prominent when the central sinus was situated to one side of the marrow cavity. Occasionally the central sinus bifurcated as it approached the distal femoral metaphysis. The central sinus was in contact with the metaphyseal venous return by anastomosing venous channels. In addition to the nutrient vein the venous system of the femur had two smaller veins leaving the distal metaphysis on its dorsal aspect.

The proximal epiphysis of the femur received arteries which entered circumferentially after passing along the sub-synovial connective tissues lying on the neck of the femur. One vessel was found fairly constantly entering the anterolateral edge of the epiphysis. Two specimens were encountered in which definite arterial casts were seen crossing the epiphyseal line.

The distal femoral epiphysis received most of its arterial supply from the abundant circulation about the knee (Figs 4 and 5). In addition an artery entered the region of the intercondylar notch. The venous return was principally by means of a vein leaving the intercondylar notch.

GROSS BLOOD SUPPLY OF TIBIA

The main nutrient artery of the tibia was found in a groove on the posterior surface of the tibia. Proceeding distally, the artery perforated the cortex very gradually and at an acute angle. At about the junction of the middle and distal thirds of the tibia the artery reached the marrow cavity. Branches continuing distally were smaller than the main division of the artery, which curved and proceeded cephalad. The general distribution of branches and the spiral path were the same as in the femur. The pattern, however, differed, so that one could easily identify the bone injected by examining the arterial vascular casts thereof.

The minor nutrient arteries of the tibia were numerous in the proximal half of the tibial shaft. They entered the cortex in the manner described previously. Occasionally they bifurcated in the mid region of the cortex (Fig 2). Having reached the marrow cavity they proceeded in the most peripheral portion of the marrow. Rarely a branch would be seen penetrating the marrow more deeply. Some arteries arborized freely but many coursed as single, fine, unbranching vessels for long distances. For the most part these arteries pro-

marrow cavity by way of the nutrient foramen. The nutrient foramen was situated posteriorly in the upper third of the femoral shaft and perforated the cortex in a centripetal direction. Occasionally there were two nutrient arteries (with individual foramina) in close proximity. After reaching the marrow, the main nutrient artery gave off small proximal branches and then curved distally. Passing distally, the artery pursued a spiral path. Branches were given off, the larger of which also took a spiral course. It was not determined whether it was natural for such vessels to spiral, or whether this

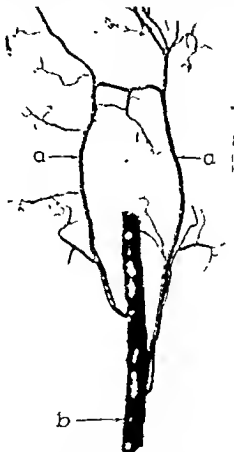


Fig. 3—Anastomosis of arteries of bone marrow. Anastomosing vessels (a) are derived from the same parent vessel (b) ($\times 65$).

was an artefact due to high injection pressures. Because of the shape of the marrow cavity, arterial branches usually originated at a fairly acute angle. While most branches assumed the same direction as the parent vessel, an occasional small vessel traveled in the opposite direction. Anastomoses were occasionally found among the medium- and small-sized arterial branches (Fig. 3). The bulk of the arterial supply of the marrow was destined for the meta

ceeded cephalad. They supplied the peripheral marrow and the adjacent Haversian systems with capillaries. These vessels were not found in the distal half of the tibial shaft.

Of considerable interest was the venous system of the tibia. An insignificant nutrient vein accompanied the artery through the nutrient foramen. The vein originated in the marrow cavity from a central sinus, which, in the distal half of the tibia, was seen to be of very small caliber and poorly developed. However, as it was traced cephalad the central sinus was seen to develop into a capacious structure with long communicating sinuses. The central sinus having reached the proximal end of the marrow cavity, was seen



Fig. 5—Side view of distal femoral epiphysis showing manner in which an artery (a) enters epiphysis ($\times 14$)

to leave the bone by way of a large vein which passed through a constantly occurring foramen on the posterior surface of the proximal end of the shaft (Fig. 6). There were also usually two additional small venous exits in the same locality.

The proximal tibial epiphysis was seen to receive an artery and vein regularly on its superior aspect just dorsal to the patellar tendon.

CAPILLARY STRUCTURE OF THE MARROW

It was unusual to obtain an almost complete filling of the venous capillary bed. When such a specimen was obtained the observer was impressed by the venous network. The cast remaining after corrosion had the shape of the marrow cavity. Obscuring all other structures was the interwoven network

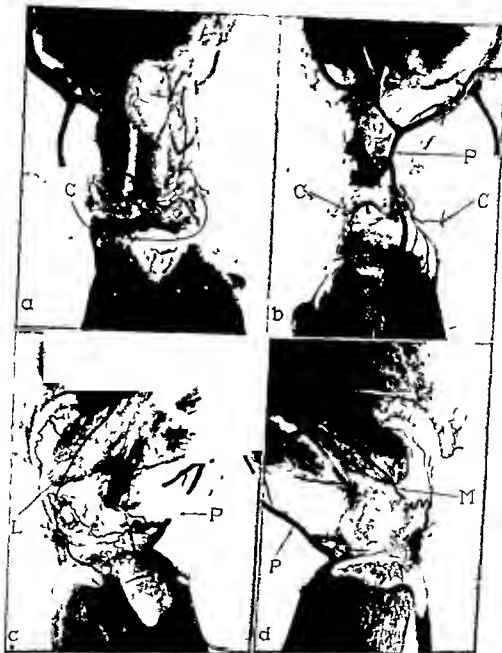


Fig. 4.—Four views of left knee partially dissected and cleared in methyl salicylate. Arterial inject. n. Anterior view (a) and posterior view (b) show (C) circumferential anastomosis. c Lateral view showing (L) lateral anastomotic circle. d Medial view showing (M) medial anastomotic circle. p Popliteal artery ($\times 5\frac{1}{2}$).



Fig 8—(a) nutrient artery showing (b) van vasorum (c) V shaped depression just proximal to mouth of van vasorum (X130)

of profuse, freely anastomosing capillary venous sinuses. These were so numerous as to make the cast feel and act exactly like soft sponge rubber. The arterial capillaries were very much finer than the venous sinuses. The venous capillary sinuses often had the shape of a cone with the arterial capillary uniting at the apex of the cone. In other instances the arterial capillary entered the flat side of a venous sinus (Fig 7). Some venous sinuses were in close proximity to large arteries of the marrow and their casts were separated with difficulty.



FIG 6.

Fig 6.—Proximal portion of tibia split longitudinally to reveal principal venous return from marrow cavity. Lib a indicate location of foramen on posterior surface of proximal portion of tibia. Partial venous injection with white neoprene. Bone colored black for contrast (X20).

Fig 7.—Cast of 1 arrow capillaries. Specimen mounted under glass cover slip. a Junction of arterial and venous capillaries. b Venous sinus (white). c Arterial capillary (black) (X265).



FIG 7.

VASA VASORUM

The corrosion specimens showed excellent examples of casts of the vasa vasorum of the marrow arteries (Fig 8). Although the vasa vasorum usually passed in the same direction as the parent artery, some took a reversed direction. Often several vasa vasorum were found in a short length of artery.

POSSIBLE DIVERSIONARY VALVES AT MOUTHS OF SMALL ARTERIES

V shaped depressions in the neoprene casts just proximal to the mouths of arterioles were sometimes found (Figs 8 and J). Inasmuch as the neoprene casts are of high fidelity, it can be assumed that the artery in this region either

main nutrient artery is injured. Their presence might explain the results obtained in experiments in which the flow of blood was interrupted in the main nutrient artery. Their absence as is the case in the distal tibial shaft might explain the slow healing of fractures in this region.

With regard to the V shaped depressions seen at the mouths of occasional small arterial branches, it is interesting to note that the apex of the V is always pointed upstream. This may signify the presence, in the wall of the parent artery, of a diversionary valve. Such a structure might prevent the full systolic thrust of blood in the large parent artery from reaching the mouth of the small branch.

The injection artefacts may also be of significance. They may indicate the course taken by extravasated fluid when a blood vessel of the marrow ruptures and may thus have clinical importance. Experimental work has shown that marrow infarcts become revascularized. However, where circulation is poor, as in the head of the femur a vascular accident of this type might possibly leave a permanent cystic lesion. Acquired impairment of circulation, as in arteriosclerosis plus a local vascular accident might also satisfy the requirements in an occasional case of idiopathic cystic bone lesion.

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dipped or was thickened. This finding was present only in some of the specimens, and then only where a small artery originated from a large artery directly



Fig. 3—Arterial cast illustrating V-shaped depression proximal to mouth of small branch (X35)

COMMENT

The anatomic arrangement of the vessels of the tibial marrow suggests significant implications. A liquid (blood) is pumped with pulsations into one end of the rigid tube (bone) which contains a thin walled reservoir (central sinus and communicating sinuses). The reservoir drains at the opposite end of the rigid tube. Thus there is a mechanical arrangement which permits transfer not only of some of the arterial pressure but perhaps even of pulsations, to the venous side of the vascular system. Such an auxiliary pump may be an important factor in the return of the blood from the lower extremities against the force of gravity while the body is in the standing position.

The minor nutrient arteries besides supplying the cortex and marrow may also be reserve structures which assume considerable importance when the

historic record of plastic surgery from the dim ages to our time, and in this article he established the fact that plastic surgery is next to the oldest of the surgical specialties

Dr Davis was associate professor of surgery (Plastic), Johns Hopkins University, visiting plastic surgeon, in charge of plastic surgery at Johns Hopkins Hospital, visiting plastic surgeon to the Union Memorial Hospital, Hospital for the Women of Maryland, and the Children's Hospital School. In June, 1946, he relinquished some of his more arduous duties and was named associate professor of surgery, Emeritus at Johns Hopkins.

Dr Davis is survived by his wife, Kathryn Bowdoin Davis, and their three children, Mrs Charles E Scarlett, Jr, Dr W Bowdoin Davis, and Howland Staige Davis. Throughout his life his intelligence, his kindly disposition, and his good humor brought hosts of friends and admirers, and no task was too great for him if it was to help a friend. This at times was made difficult by overwork but was overcome by the sunshine of his kindly disposition. He passed on quietly Dec 23, 1946 after a full day's work, leaving many, many regretful friends.

—Viray P. Blau

In Memoriam

JOHN STAIGE DAVIS

1872-1946

IN THE death of John Staige Davis the Guild of Plastic Surgery has lost its mentor and its first dean.

Dr Davis was born Jan. 15, 1872, in Norfolk, Va. He was the only child of the late Colonel Wm. Blackford Davis, U. S. Army, and of his wife, Mary Ann Davis, daughter of John

Lyons, N. Y., and graduated from the Sheffield Scientific School at Yale University in 1895. He entered Johns Hopkins Medical School in the fall of 1895 and graduated in 1899, becoming a resident house officer in Johns Hopkins Hospital, serving under Dr. Osler, Dr. Halsted, and Dr. Kelly. Later he became resident surgeon at the Union Memorial Infirmary under Dr. J. M. T. Finney where he remained for three years.

Dr. Davis was a keen observer, a seeker after facts, and a good clinician. For ten years he carried out research problems in the Hunterian Laboratory of Experimental Surgery and published a number of articles dealing with the results of his investigations. He was the author of *Plastic Surgery, Its Principles and Practice*, and throughout the years he published some seventy odd papers on plastic surgery in various medical journals. He was on the Editorial Board of *Surgey*, was a founder member of the American Board of Surgery and of the American Board of Plastic Surgery, at one time was first vice president of the American Surgical Association, president of the Southern Surgical Association, president of the American Association of Plastic Surgeons, and was a Fellow of a number of related bodies. He was also a founder

of the face wounded, so prevalent in trench warfare, Captain Davis was one whose advice was first sought in the details of carrying out this assignment. When, after the war, it was realized that the same care was needed for a vast number of similar injuries in civil life, the Advisory Board for Medical Specialties of the American Medical Association was petitioned for authority to form an independent specialty board for Plastic Surgery. The authority was granted and Dr. Davis was chosen as the Board's chairman, a position he held until a short time before his death, and the successful establishment and operation of this Board was largely due to his sound judgment in difficult circumstances and his impeccable social and professional record. His Presidential Address for the Southern Surgical Association in 1940 is a classical

historic record of plastic surgery from the dim ages to our time, and in this article he established the fact that plastic surgery is next to the oldest of the surgical specialties

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Book Reviews

The Differential Diagnosis of Jaundice By Leon Schiff, M D Pp. 313 Chicago, 1946
The Year Book Publishers, Inc

This is an excellent monograph. The author adheres closely to the objective as set forth in the title. Schiff, an experienced clinician, has presented in surprisingly few pages a very clear discussion of the clinical and pathologic disorders accompanied by icterus. The diagnostic features of case history, of physical findings, and of pertinent laboratory data are skillfully blended.

The literature of the last decade is very completely covered, each citation of a reference serves to emphasize a practical clinical feature without, however, interrupting the continuity of the paragraph. The monograph is clear, concise, and pleasant to read.

Many of the laboratory procedures so useful in the differential diagnosis of jaundice are quite recent. Anyone interested in them must refer to a number of articles scattered throughout scores of journals. This book describes the most useful of these so called tests of liver function, not in the fashion of a laboratory manual but in a manner that is certain to prove appealing and instructive to the practicing clinician. Carefully weighing the merits and limitations of these laboratory aids, the author amply demonstrates the fashion in which they can be of great help when properly correlated with findings at the bedside. The inclusion of concise case histories brings out exceptionally well the types of clinical approach to diagnosis. The inclusion of an appendix containing specific laboratory directions for the tests that the author has found useful in clinical practice adds to the value of the book.

The chapters on calculous and cancerous jaundice contain a great deal of practical value to both surgeon and internist. The apparent frequency with which jaundice appears to develop following transfusions of plasma and whole blood or the administration of blood products makes it essential that surgeons familiarize themselves with this relatively new form of parenchymal liver disease homologous serum jaundice. This subject is dealt with adequately in a special chapter.

The surgeon will find this concise volume exceedingly useful. It is highly recommended.

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Original Communications

Society of University Surgeons

THE RESPONSIBILITY OF THE UNIVERSITY SURGEON

ELLIOTT C. CUTLER, M.D., BOSTON, MASS.

THIS is a happy occasion for me and I am highly sensible of the privilege of being allowed to welcome the Society of University Surgeons to this medical school and the hospitals about it. You represent at a top level the steady development of surgery in our country.

These buildings, first occupied in 1906, were the seat of my medical education, my class was one of the earliest to secure its four years of education in these, then, new halls. These buildings were the result of careful planning, chiefly through the vision of J. Collins Warren, then Moseley Professor of Surgery, and Henry P. Bowditch, Professor of Physiology. The land, when purchased, was also planned to be the site of the future Peter Bent Brigham Hospital and the Children's Hospital. By the time I was graduated, the new Peter Bent Brigham Hospital was finished and although I had planned to go to the Johns Hopkins Hospital for postgraduate training, that move to a new environment never came, since Harvey Cushing, under whom I desired to train, had moved to Boston when I was a senior medical student and began his work in the new hospital the year I graduated. The Children's Hospital was then situated on Huntington Avenue but was built adjacent to the school in 1914. These last thirty-eight years have passed rapidly and yet during them great changes, especially in the education and training of the surgeon, have occurred. Representative of these changes is the fact that at the time my class graduated, 1913, only two hospitals, the Johns Hopkins Hospital and the Peter Bent Brigham Hospital, had an organization that could have qualified surgeons for membership in this group.

Throughout these years, and beginning perhaps ten years before my advent to medicine, there had been going on great changes in the educational side of our profession. These changes set higher and higher standards and delivered large

Presented at the meeting of the Society of University Surgeons, Boston, Mass., Feb. 13-15, 1947.

numbers of vigorous and stimulated students from medical schools to hospitals where they gave vent to their demands for better medical societies, better medical journals and higher and higher standards.

By reason of the clamor of the many young assistants in schools and hospitals for an opportunity to submit their work publicly the American Society for Clinical Investigation was formed in 1908 and in 1923 I became a member. Unfortunately, only a few surgeons joined or were permitted to join and so the demand for a similar surgical group became a frequently belabored issue. At the same time the output of trained young surgeons vastly increased and there was insufficient space in the existing journals for the publication of their writings. This latter struggle ended with the establishment of the journal *SURGERY* in 1937 but no over-all society for junior surgeons arose. Meanwhile surgeons travel clubs and surgical groups increased, modeled more or less on the original example. The Society of Clinical Surgery thus absorbing part of the demands of young surgeons for an opportunity to present their work and discuss their problems.

During the period that all this flux was taking place and even antedating it was the mounting evidence in the Council on Medical Education of the American Medical Association so long and consistently led by A. D. Bevan that medical education itself needed improvement. This culminated in the famous report on medical education in the United States and Canada by Abraham Flexner published in 1910. Later open criticism springing up that membership in the American College of Surgeons did not necessarily carry the implication that all its Fellows were good surgeons. This sort of milling about led to the formation of the American Board of Surgery in 1937 and finally the bed was set for your birth in 1938.

I had the opportunity to live through and participate in many of the discussions and much of the work that led to the changes already noted. I took a firm stand in defense of the younger surgeons when they began to be turned down in numbers by the American Society for Clinical Investigation. Some relief was had with the establishment of the American Association for Thoracic Surgery in 1917 since a good many young surgeons were working in this field and the publication of the journal of this association in 1931 gave an added outlet to surgical papers. I long thought the early years of this association gave the best meetings in surgery in our country and found them frequently preferable as intellectual food to the meetings of the American Surgical Association. It was now clear that Surgery in this country had become finally separated from its position as a handmaiden of Medicine. The surgeons had become quite independent and demanded their own societies, their own journals and for a time paid less and less attention to their medical colleagues at least in forming medical societies although the joint investigations of young surgeons and their internist colleagues increased. The whole change went on gradually and was no doubt in part due to the better type of students going into medicine and the better education given to them although special emphasis must be placed upon the fact that the heads of the great surgical clinics were now eagerly encouraging investigative

work among their assistants and once the youngsters had done their work they demanded a proper outlet

You are as you see the product of many genes and chromosomes for at least you are supposed to represent the best educated and trained surgeons in our country. Although I was among those earliest interested in your formation and am desirous that you should hold a leading position I have a strong dislike of one generation dictating policies to its successor even father to son. However I do hope you will maintain very strict qualifications for membership. Letting down the bars for admission is sure to damage your ability to influence American Surgery. Perhaps I am influenced by my own long training of six years before I became resident surgeon at the Peter Bent Brigham Hospital. In any case I do not believe that full training as a surgeon can be hurried and by such training I mean an individual who is at least able to conduct with safety and general excellence surgical procedures in any part of the body although he need not claim great proficiency in but one field. It was my idea that a resident surgeon would be quite competent to run a large surgical service in the absence of his chief.

But your future will not only deal with technical advances for these often are the simplest of your responsibilities. In your hands also will repose responsibility for the numbers of doctors required by your country, the methods of nursing education that will supply the necessary number and quality of nurses for our whole people and for the moment while so many of you are fresh from military service in ways and means of securing a better organization for the medical defense of your country than now exists. This last mentioned task I have deliberately called medical defense since none of us can predict whether or not there will be a joint merged medical service for the Armed Forces. At any rate it must be organized from the viewpoint that total war involving equally civilians and the military personnel will begin with the first act of aggression and with the understanding that the care of all the people then becomes a federal responsibility.

Regarding the numbers of physicians and surgeons available to our people it would appear that two tendencies are at work. (1) the fairly strict limitation placed on the number of graduates from our medical schools both by the failure of the present schools to enlarge our classes a matter depending upon endowment and availability of teachers and the rarity with which new schools are formed and (2) the natural increase in population (several millions during the war years) and the increased utilization of doctors not only by the public at large itself but by government and industry. We must evaluate that the Veterans Administration alone has taken 5 000 doctors out of the practicing number of physicians and surgeons and that industry is gradually caring for its own people and thus diminishing the number of physicians left for the population. Also for the duration of the present crisis and for the care of our still enormous Armed Forces several thousands of physicians and surgeons must be kept in that form of service. Surgeons in charge of academic posts or large clinics know that they have innumerable demands for young surgeons which they cannot fill.

and many doctors are seriously overworked. Why should the doctor work sixty hours a week and the laborer forty? You must cogitate upon these matters and lend the weight of your united opinion as to what is the best solution for your country.

The nursing situation is even worse. Over the last twenty years the profession of nursing, supported by idealistic and wealthy women, has sought for ever increasing educational demands, more as a part of the emancipation of women than in relation to their responsibility for the care of the sick. What will obviously dictate the nurse in the future is what the public must have to care for the sick and it is time that the profession of medicine as a whole took up this problem and did not leave it entirely in the hands of nursing educators, for our responsibility is really for the care of the sick and we cannot set aside that important fragment delegated to the nurse as if it now were something we could leave to others. Obviously, the five year nurse with a degree is not going to nurse the sick public in his home. Someone must do this. And someone will do it, irrespective of what the nursing educators feel. Here is a major problem for your evenings.

This partial recital of your responsibilities is given to whet your appetite. Undoubtedly these and other matters have long since claimed your energies and thoughts. Education and a conscience are rugged taskmasters, driving us, when most in need of rest, to new labors. And when the work is at its greatest, then you in turn must hand it on to your disciples.

The list of titles to be presented in your three day meeting here bears strongest testimony to your accomplishments. On your shoulders will shortly fall the mantle of American Surgeon. We who are so jealous of your prerogatives and position know the future of our art and science is quite safe in your hands.

DOES MEDICAL INSURANCE ENDANGER THE RESIDENT SYSTEM OF TRAINING SURGEONS?

HERMAN E. PEASEL, M.D., ROCHESTER, N. Y.

(From the Department of Surgery, University of Rochester School of Medicine, and Strong Memorial Hospital)

DURING the last decade we have seen a steady decline in the number of ward patients available for treatment by residents in surgery. This decline reached a climax during the inflationary period of the war, but began during the depression. It now coincides with an increase in applicants for residencies due to the advice of the American Board of Surgery that resident training is preferable for certification. This creates the conflicting situation of more applicants than ever before, with fewer patients available for their training.

The decrease in the admissions to the wards and coincident increase in semi-private and private patients is of such vital concern to the teachers of surgery that it warrants careful consideration. It was decided to study the possible causes for this in the Strong Memorial Hospital, which is fairly typical of many teaching hospitals in this country.

The Medical School of the University of Rochester has three affiliated hospitals: the Strong Memorial Hospital, which it owns, the Rochester Municipal Hospital, which it operates under contract with the city, and the Genesee Hospital, with which it is associated by agreement. The Strong Memorial Hospital is the only one of these that is designed, constructed, and operated purely as a teaching hospital. It began with 193 clinic beds arranged largely in four-bed cubicles, and 30 semiprivate and private beds. The patients were cared for by a small, full-time staff, as were those in the 282 beds of the Rochester Municipal Hospital, which is an integral part of the medical school unit. This gave a total of 475 ward beds available for resident training.

In 1931 a floor of 14 private rooms was opened in the Strong Memorial Hospital. In 1934 semiprivate patients were admitted to the four-bed cubicles previously occupied only by clinic patients. These were used for teaching, but the attending physician became responsible for the care. In surgical cases this meant that the attending rather than the resident surgeon did the operation. In 1941 a private wing was completed, and 60 of its 120 beds were opened.

The admissions were tabulated from 1934, the year when semiprivate patients were admitted to the wards, up through 1945. The result is charted in Fig. 1, where it is seen that the ward patients dropped from 68 to 17 per cent, with a corresponding increase of semiprivate and private patients from 32 per cent in 1934 to 83 per cent in 1945. During this time the census of the Rochester Municipal Hospital declined somewhat, and the character of the work changed.

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it is mentioned here only for that reason. Obviously this could not affect a comparable trend in other hospitals in this community nor those in other cities. The clinical departments of the medical school began in 1926 with small full time staffs. The depression with its loss of return from endowment made it difficult to enlarge the clinical staff on a full time basis. In 1932 full time clinicians were permitted to amplify their income from patients fees according to the method suggested by Halsted* and often called the Harvard system. Others became part time but retained geographic full time.

This introduced private practice and the need for private and semiprivate beds to support the staff in the teaching hospital. Whether or not it affected the trend of increase in private patients at the expense of the wards cannot be evaluated. It coincided with other economic factors that flowed in the same direction.

Hospital insurance began in Rochester in 1935 with 20 500 subscribers and grew steadily until it had enrolled 256 000 members in 1945. This is plotted in Fig. 1 on a percentage of the population of the city and corrected as well as possible for out of town contracts. It is the only statistical comparison that could be used to demonstrate the growth of medical insurance factors. There are others less susceptible to analysis. The state of New York during this period has increased state aid for crippled children converting many patients with congenital or acquired deformities into the semiprivate group. Maternity benefits derived from state or national sources have done the same. Workmen's compensation has broadened its coverage and all these patients are semiprivate. The Veterans Bureau provides hospitalization for emergency cases or service connected disability in private hospitals on a semiprivate basis. If dependents are added then between 30 and 40 million people will be affected.

The steady growth of hospital insurance in Rochester has resulted in 75 per cent of the population being enrolled. These contracts provide for semiprivate care and have been the greatest single factor in the conversion of ward to private patients. Elimination of hospital costs leads many people to have their own doctor and pay his fee. There has been a less extensive but equally steady growth of hospital insurance in the nation so that at present Blue Cross coverage is provided for 24 000 000 people. Medical indemnity or care contracts are held by 4 000 000 people. Large industries are providing hospital and medical contracts to their employees as a condition of employment. Finally, attention is being paid for compulsory health insurance. If this is enacted there will no longer be any ward patients.

How can we continue to train surgeons under these circumstances? The resident system provides after five or six years probationary training under supervision a period of at least one year when the resident is largely responsible for the operations done on the clinic patients. This is the crux of the method for without it confidence, judgment and technical skill are difficult to acquire. The resident in medicine or pediatrics may be trained on private patients but

* There is however a compromise which even at present (1944) is altogether feasible. Let the surgeon be permitted to accept remuneration for services to certain patients operated upon in the hospital which the only really practical controls. His consultations and operations will all take place at the hospital. Halsted W. S. The Training of the Surgeon Johns Hopkins Bull. 13: 26, 1904.

with fewer acute disorders in the younger age groups to more chronic diseases in the older age groups. It was found that in other general hospitals in this community the same shrinkage in the ward admissions had occurred. Conversations with surgeons in other cities revealed that this trend was widespread.

The three explanations which were considered as possible causes of this decline of ward and increase of private patients were increased national income from a war boom, change in financial relation of the teaching staff to the medical school, and growth of medical insurance. In Fig 1 the national income*

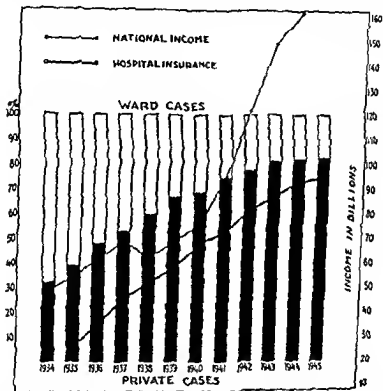


Fig 1—The per cent of private patients admitted to the Strong Memorial Hospital from 1934 to 1945 is charted in black. It is seen that the growth of hospital insurance correlates better than does the national income with this increase in private patients.

in billions of dollars, corrected for relief payments, is charted. This curve follows that of the private patients for the first four years but then ceases to correlate with it. It appears significant that the decline of ward patient census started in the depression. This makes it appear probable that a more profound long range change is responsible. It is unlikely that the end of the inflationary war prices or another depression will correct the condition although it is granted that these may modify it.

During the period studied changes were made in the financial relations of the attending staff to the medical school. Some feel that this had influence and

*Obtained from the Statistical Abstract of the United States

SURGICAL MANAGEMENT OF LARGE DEFECTS OF THE THORACIC WALL

HERBERT C. MAIER, M.D., NEW YORK, N. Y.

LARGE defects in the thoracic wall may result from the radical resection of tumors from areas of radiation necrosis and from trauma. Although the chest wall may be extensively involved by infection, destruction of the entire thickness over a large area is uncommon. If the loss of tissue of the thoracic wall involves only the skin, subcutaneous tissues, and extrathoracic muscles, the principles of management are similar to those followed when treating defects in other portions of the body. When the bony or cartilaginous structures are destroyed or removed over a considerable area, other problems peculiar to the thoracic cage are encountered. If the defect extends into the pleural cavity, the problem of an open pneumothorax must also be met.

The resection of several ribs, cartilages, or a large segment of the sternum deprives that portion of the chest wall of its normal stability and results in paradoxical motion. The degree of abnormal mobility on respiration will vary with the location and extent of the defect and will also be influenced by the thickness of the soft tissues and other factors such as the presence of pulmonary emphysema. If the resection of the lesion of the chest wall requires the sacrifice of the parietal pleura, a flap of tissue must be made available for an airtight closure of the opening. Skin grafting alone would obviously be inadequate in such cases.

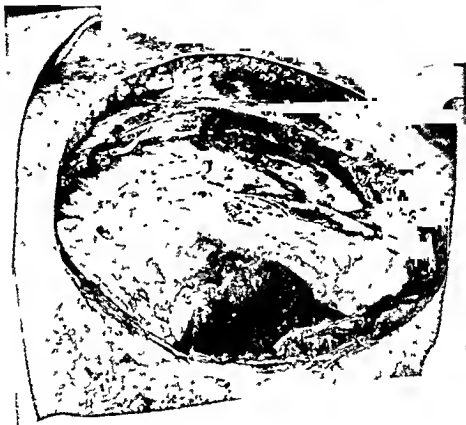
Local recurrence of carcinoma following radical mastectomy for cancer of the breast may merit surgical excision if there are no evident distant metastases. The value of such secondary operations is considerably enhanced if the procedure is of a radical type. Often the entire thickness of the thoracic wall from the skin to and including the parietal pleura should be excised. If the surgeon compromises in the extent of the excision in order to avoid a large defect or opening into the pleura, less satisfactory results will be obtained. When the resection includes the cartilages, ribs, intercostal structures, and parietal pleura, a flap of skin and subcutaneous tissues down to the deep fascia should be mobilized from adjacent areas and swung over the defect as a pedicle flap. Since the tissues in the region of the previous mastectomy wound are rather fixed and somewhat fibrotic, this pedicle flap should be fashioned from tissue which was not in the field of the original mastectomy operation. A flap for the central part of the thoracic wall may be obtained by mobilizing the tissues forming the medial portion of the opposite breast. The tissue of the anterior abdominal wall with a pedicle laterally may be utilized for defects in the lower anterior thoracic region and pedicle flaps from the axillary region may be used for the closure of defects in the lateral portion of the thoracic wall.

If intensive radiation therapy followed the original radical mastectomy, the situation is more complicated. None of the irradiated tissue can be satis-

in surgery, gynecology, and obstetrics the technical procedure of operation or delivery is the focus of the management. The resident in surgery must have clinic patients if he is to be adequately trained. He can be carried far, but never finished, if private patients only are available. The assumption that medical insurance is socially and economically sound leads to the belief that its influence will increase, and so our clinic patients will further decrease.

It would be possible to train surgeons by resorting to the preceptorial method of assistantship. This time honored means is adequate, but never accomplished the results of the resident system. Occasionally private patients may be operated upon by the resident staff, but unless this is done with the patient's knowledge and consent it is dishonest. Such a haphazard arrangement cannot be used as a basis for a training program. The final solution is to change the method of practice in teaching institutions so that patients come to the hospital or clinic rather than to the individual surgeon. This requires the entire staff, junior and senior, to be full time, salaried, and practicing as a group. Responsibility for care is then delegated on a basis of medical need rather than financial standing. This method has been tried in one medical school, and has not only permitted the care of private patients by the resident staff, but also has allowed the restoration of full time without prohibitive expense to the University. Such a change has disadvantages, but the time may come in the not too distant future when the surgical teacher must choose between the present method of individual practice and the resident system of training surgeons. It appears doubtful that he can retain both.

attempts to improve the situation by merely resecting the obviously devitalized tissue or sequestering bone or cartilage are often disappointing. The necrosis may extend following such a procedure. The area of radiation is usually too large to permit the resection to be carried into the healthy unirradiated tissue at the margins. Moreover the effect of the irradiation extending through the entire depth of the tissues eliminates the prospect of obtaining a supply of healthy granulations from the depths of the wound.



The procedure which has been most successful in managing such large irradiation defects of the chest wall has been first to improve the wound as much as possible by careful frequent dressings and local application of antibiotics and second to excise the dead tissue and at the same operative procedure to swing in a flap of tissue large enough to cover the entire defect without tension (Figs 3 and 4). This flap must not contain any irradiated tissue or tissue whose blood supply is otherwise impaired. If the defect or

factorily employed for a pedicle flap and much tissue may have to be excised in order to permit a flap of normal tissue to be swung into the site of the operative defect.

Additional difficulties may arise when extensive radiation necrosis of the thoracic wall has occurred. Under such circumstances devitalized tissue forms the bed of the large ulceration. Portions of cartilage denuded of perichondrium, and ribs denuded of periosteum, may project into the wound. Necrotic

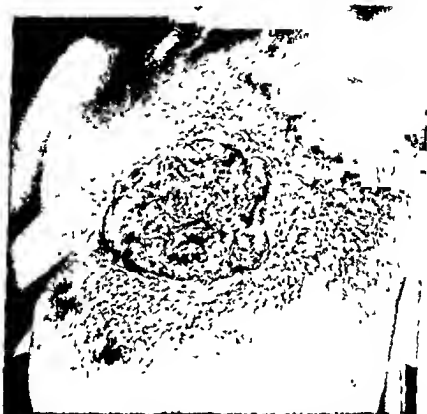


FIG. 1.—Large cancer has in area of severe radiation dermatitis following radical resection. The tumor was ulcerated and foul smelling and it extended through almost the entire thickness of the thoracic wall. The heavily irradiated skin began to ulcerate over ten years after radiation therapy had been given.

fascia and tendinous structures may slough over a long period of time (Figs. 5 and 6). In some cases the radiation necrosis extends through the parietal pleura and may result in a collapse of the lung with pneumothorax or empyema or may lead to direct ulceration into the lung with destruction of pulmonary tissue and the development of a bronchial fistula. Since the underlying lung is also the seat of radiation pneumonitis and fibrosis healing and resistance to infection is impaired. When the radiation effect has reached a degree which prevents healthy red granulations forming in an ulcerated area,

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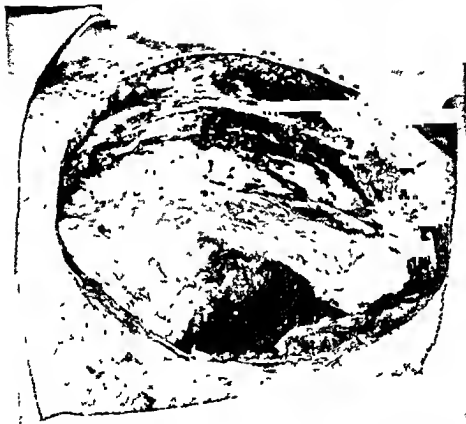


Fig. 2—Same patient
tent's head is at the right;
pleura was removed on one;
the sternum to the anterior
The pericardium is widely ex-

posed. Pa-
rietal
body of
ter space
sible

The procedure which has been most successful in managing such large irradiation defects of the chest wall has been first to improve the wound as much as possible by careful frequent dressings and local application of antibiotics and second to excise the dead tissue and at the same operative procedure to swing in a flap of tissue large enough to cover the entire defect without tension (Figs 3 and 4). This flap must not contain any irradiated tissue or tissue whose blood supply is otherwise impaired. If the defect or

Fig 3

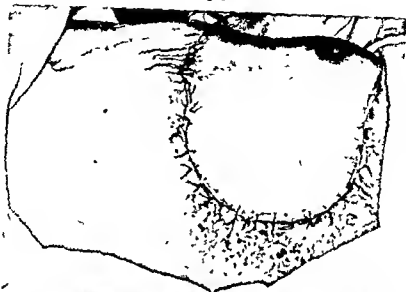


Fig 4

FIG. 3.—(Photographs of same patient as shown in Figs. 1 and 2 taken after the right breast and skin of the right upper quadrant had been mobilized and swung over the defect on the left side of the thorax. Patient's head is at the right and the view is toward the left.

FIG. 4.—(Photograph showing radiation reaction is visible in the posterior portion of the axillary

excision of the chest wall has extended into a free pleural space it is mandatory to suture the flap in place and close the entire wound without drainage to avoid a sucking chest wall wound. The collapsed lung is immediately expanded by removing the residual air through a catheter, which is then withdrawn. If the pleural space has not been entered a drainage tube to evacuate serum under the flap may be desirable. The local and systemic use of antibiotics is most important in aiding the healing of such a flap placed over unhealthy irradiated tissue in the presence of marked contamination or gross infection. If the flaps have an excellent blood supply and are not under tension surprisingly good results may be obtained. Flaps fashioned from the breast on the opposite side have been most satisfactory in closing such large defects (Fig 7).

When a malignant tumor causes extensive involvement of the chest wall requiring the sacrifice of all of the tissue from the skin to the parietal pleura a large defect results which requires immediate airtight closure so that no opening into the pleural space remains and so that the lung can be immediately reexpanded (Fig 2). In one of my cases a cancer had developed secondary to radiation dermatitis following mastectomy (Fig 1). Thus a further difficulty arose because of the irradiation changes in the adjacent tissues in the axillary region, lateral thoracic region and even extending to the upper abdominal area. Under such circumstances the only tissue available which is not irradiated is that on the opposite side of the body and here particularly the breast of the opposite side is most satisfactory.

The majority of the cases of defects of the thoracic wall that I have encountered have been in women because carcinoma of the breast has been the most common lesion which eventually resulted either directly or indirectly in the sacrifice of portions of the chest wall. Therefore the remaining breast on the opposite side has been frequently the most satisfactory source of a flap for closure of the defect. By mobilizing the breast completely at its lower margin and to a considerable extent along both the axillary and medial borders the breast can be displaced considerably and yet maintain an excellent blood supply through its upper and axillary attachment (Fig 3). The defect created by the displacement of the breast toward the opposite side of the anterior chest wall can readily be closed without tension by mobilization of the subcutaneous tissue in the lower axillary and upper abdominal areas. An additional incision may be required for permitting a satisfactory advancement of these latter flaps (Fig 4).

When it is planned to utilize the opposite breast to cover a large defect of the anterior thoracic wall the type of incision recommended will depend on the size of the breast. If little mammary tissue and fat are present the breast will cover little more than an area corresponding with its dimensions. If a pendulous breast is present incisions can be made so as to spread the breast tissue out over a large area. In either case the essential principles are to make a curved incision from the lower medial aspect of the defect caudad to the opposite breast extending laterally to the anterior axillary line where it

curves up in the direction of the anterior fold of the axilla. The distance that the incision is carried up toward the axilla varies with the degree of mobilization required. The incision is deepened throughout down to the fascia covering the extrathoracic muscles. The pectoralis major will form almost the entire base of the wound. The breast is freed from the pectoral fascia by combined sharp and blunt dissection. Care is taken not to interrupt needlessly any blood vessels. When adequate mobilization has almost been obtained division of additional blood vessels can usually be avoided if blunt



Fig. 1. Photograph shows area of gallbladder necrosis following steps of radiation and radical mastectomy. Note the large protrusion present on the opposite side which was later used for plastic closure.

dissection with freeing of vessels without division is employed. It is equally important, however, to free the flap sufficiently to avoid any tension when the suturing is done later. The breast will have to be mobilized to some extent along its medial border and some of the perforating branches from the internal mammary vessels will require ligation.

If the defect to be closed extends to the anterior axillary line and the breast of the opposite side is small and flat the incision should be curved

Fig 6

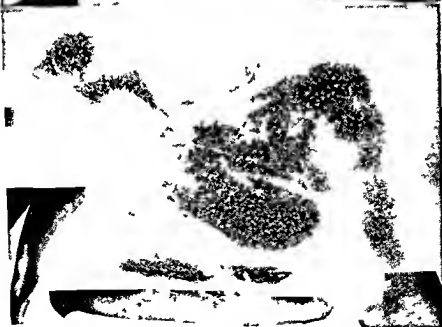


Fig 7

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pendulous oppo
s te breast was ut lized to c ose the en re defe t. Primary hea ng oc urred

down over the upper part of the abdomen so that an adequate sized flap is obtained (Figs 3 and 4). In such a case the skin of the upper abdomen will be eventually placed in the axillary region of the opposite side. When the breast is pendulous, the incision should be made in the inframammary fold. A secondary incision at right angles to the inframammary one is made in the nipple line from the lower aspect of the areola to the inframammary incision, thereby transecting the middle of the lower half of the breast. This procedure will permit the pendulous breast to be spread over a considerable area (Fig 7). The outer portion of the breast will cover the ipsilateral anterior chest wall while the medial half of the breast is utilized to close the defect on the contralateral side. The lower medial quadrant of a pendulous breast may under favorable circumstances, be brought without tension as far as the mid axillary line of the opposite side. In such a case the nipple may then be located near the midline in the region of the xiphoid (Fig 7). I have not removed the nipple in order to avoid as much as possible all unnecessary interference with blood supply. If it were desired to improve the cosmetic result this might best be done perhaps at a later date.

Resection of a tumor of the chest wall often requires removal of the ribs intercostal structures and parietal pleura en masse over a considerable area. If the skin and subcutaneous tissues can be preserved the skin incision should be so planned that it will not overlie the central or weakest portion of the wound. If the extrathoracic muscles can be spared, the incision through the muscles should also be so placed that it does not underlie the skin incision. A staggered layer closure is advantageous. A flap of fascia lata should be sutured into the defect in the chest wall as advocated by Watson and James.¹ The fascia is attached to the parietal pleura at the edges of the defect. It can be utilized whether or not the parietal pleura is removed but this is not necessary when the periosteum of the ribs remains. When all tissue from which bony regen-

lata in the

When several

strip of the periosteum of the rib at the outer margin of the resection. The periosteum is divided parallel with the rib margins and a subperiosteal resection of the edge of the rib away from the tumor is performed. The periosteum is later again divided on the inner aspect of the rib. By this maneuver a portion of the periosteum is preserved although the rib is resected with the periosteum attached on the side of the tumor. This procedure should not be employed if it interferes with removal of the thoracic wall lesion by a safe margin.

Any repair of the thoracic wall which does not employ bony structures or periosteum from which bone can regenerate fails to give an ideal result. Permanent paradoxical motion with respiration and bulging on coughing or straining may be noted. Therefore whenever possible periosteum or segments of rib or cartilage should be used in the closure of the defect. The employment of a foreign body such as tantalum plate has been unsatisfactory because proper anchorage and imbedding has not proved feasible. It is difficult to immobilize

the metal plate in a moving chest wall In a discussion of hernia of the lung Maurer and Blades¹ reported that the best result in closure of a defect of the chest wall is obtained by using rib periosteum, and muscle They found that the most satisfactory repair of average sized defects was obtained by using a periosteal flap developed from ribs immediately above and below the margin of the hernial orifice In some cases ribs at the margin of the defect were cut tangentially and then displaced upward or downward and fixed to the rib stump of an adjacent partly resected rib These displaced ribs helped to narrow the defect and the periosteum from these ribs could be sutured to one another to further lessen the space These maneuvers could not be employed in some of the huge defects that we have encountered and in such cases one must be content with a closure which does not have the stability of the normal thoracic cage If a large defect of the entire thickness of the thoracic wall is present combined with an empyema a combination of thoracoplasty and the use of a full thickness flap of the chest wall may be employed as in the case reported by Priolau² He closed a defect over the precordium by making an intercostal incision through the full thickness of the chest wall lateral to the defect at its upper and lower margins Because the paravertebral portion of the ribs of this area had previously been removed subperiosteally, it was possible to slide this full thickness flap over the precordium and hold it in place by sutures to the sternum Because such a flap contains periosteum later bone regeneration can occur and the chest wall may therefore become firm in contrast to the flaccidity of the chest wall resulting when only a flap of soft tissue is employed

The result of the closure of large defects of the thoracic wall by utilizing the tissues of the opposite side of the anterior thoracic wall has been so satisfactory that it has seemed to me that the method might be employed more widely in patients with much less extensive defects in the thoracic wall

Following radical mastectomy for carcinoma of the female mammary gland defects of varying size in the skin and subcutaneous tissues of the anterior thoracic wall may occur Skin grafts are usually employed to cover the residual defect The results in general are very satisfactory If the carcinoma is located near the inner margin of the breast the area requiring skin grafting may overlie the costal cartilages In this type of case costal chondritis occasionally develops because of an incomplete take of the graft and denuding of the cartilage of its perichondrium An alternative method to skin grafting is the mobilization of the skin and subcutaneous tissues across the sternum and to some extent along the mesial portion of the opposite pectoral muscle which may enable such a wound to be closed without tension and without grafting The degree to which this undermining can be carried out without danger of impairing the blood supply to the skin margin depends on how close the dissection is carried to the skin in the performance of the radical mastectomy Resection of the chest wall combined with radical mastectomy may be indicated in some cases in which the carcinoma of the breast is fixed to the deep tissues

SUMMARY

The problems encountered in the management of large defects of the thoracic wall are discussed. Methods of improving the stability of the chest wall in the presence of such defects are reviewed. The utilization of the opposite breast for the closure of these large wounds which may be associated with much loss of tissue and large openings into the pleural cavity is illustrated.

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THE USE OF A PROSTHESIS TO PREVENT OVERDISTENTION OF THE REMAINING LUNG FOLLOWING PNEUMONECTOMY

A PRELIMINARY REPORT

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FOLLOWING total pneumonectomy there are two commonly used methods of dealing with the empty pleural cavity. When drainage of the cavity becomes necessary because of infection a thoracoplasty must be done to obliterate the empyema cavity. The lateral chest wall is made to fall in and approach the mediastinal position (Fig. 1). If the chest wall is closed without drainage in the absence of infection the pleural cavity gradually becomes filled with serum. Over a period of time the serum either is absorbed or clots and contracts. As the contraction of the clot occurs the mediastinum is pulled over to approach the position of the lateral chest wall. This results in considerable overdistention of the remaining lung, a condition referred to as compensatory emphysema (Figs. 2 and 3).

It has been our impression that those patients who were so unfortunate as to develop infection and thus required a thoracoplasty had a better end result on the whole than those patients who did not have a thoracoplasty and thus developed compensatory emphysema of the remaining lung. Courmand and Berry have shown that this is a compensatory emphysema in an anatomic sense only and not in a physiologic sense for they have demonstrated that such a lung does not function as well as a lung of normal size. They found that both in children² and in adults¹ the exercise tolerance was greater in those patients in whom overdistention of the lung was prevented by thoracoplasty. It would seem therefore that an elective thoracoplasty should be done routinely following pneumonectomy in order to maintain the greatest pulmonary efficiency.

On the other hand it is known that patients usually get along fairly well with this emphysema of the remaining lung even though their activity may be somewhat curtailed. The thoracic surgeon hesitates to suggest a major procedure such as an elective thoracoplasty following pneumonectomy if it can be avoided. This is especially true of the patient operated upon for malignancy whose life expectancy may not be great in any event. We have not recommended elective thoracoplasty in such circumstances but have decided to recommend it to the patients operated upon for benign lesions who in our opinion had a long life expectancy. However for one reason or another we have found that more often than not we failed to do the elective thoracoplasty, a circumstance which we realize is not in accord with our best physiologic judgment.

It seemed desirable to attempt to prevent overdistention of the remaining lung by some means simpler than a thoracoplasty. Preliminary experiments with the use of a noncompressible prosthesis to fill the pleural cavity following pneumonectomy indicate that this may be a satisfactory method of dealing with the problem.



Fig. 1.—One year following right pneumonectomy and thoracoplasty in a 54 year-old man for carcinoma of the lung. The mediastinum is maintained near the midline and severe overdistention of the remaining lung is avoided.

In searching for prosthetic material to serve as a space taking object in the pleural cavity we have considered oils, metals and plastics. It is apparent that the ideal material should fulfill certain requirements: (1) It should be able to conform approximately to the size and shape of any pleural cavity, (2) it should not increase the incidence of infection, (3) it should cause little or no foreign body reaction in the tissues so that it would become encapsulated, (4) in the event of infection it should be easily removable through a small opening in the chest wall, and (5) it should be light in weight.

Some type of oil or paraffin would seem to be ideal except that these hydrocarbons may cause considerable tissue reaction. Oleothorax in the collapse therapy of tuberculosis has never been popular because of the unpredictable

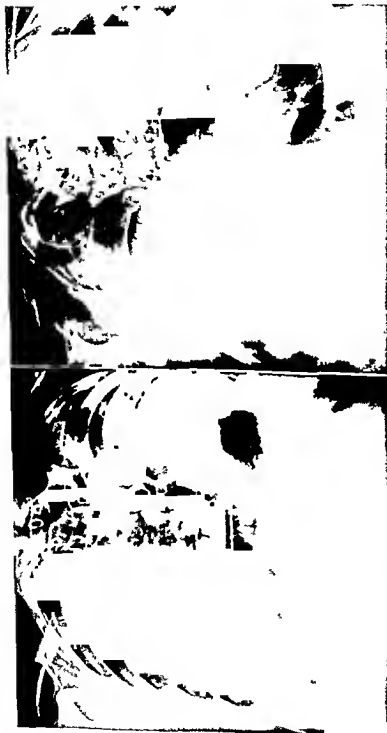


Fig 2

Fig 2—Severe overdistention of the right lung following left pneumonectomy for bronchial adenoma in a 60 year old man. Barium in the esophagus shows it to be pulled over to the left. The right lung approaches the left side of the chest wall.

Fig 3

Fig 3—Severe overdistention of the left lung following right pneumonectomy for carcinoma in a 58 year old man. This man has had a five year cure and complains only of some dyspnea on exertion.

irritation of the pleura with little effusions which occur in certain individuals. Likewise paraffin has never been entirely satisfactory as a space taking material to fill the cavity of an extrapleural pneumothorax. Nevertheless oil has been used in at least one patient for the specific purpose of preventing mediastinal shift following pneumonectomy.⁴



Fig. 4.—A dog two months following left pneumonectomy without the use of a prothesis. The mediastinum is over against the left side of the chest wall and the overdistended right lung fills the lower part of the left side of the chest cavity.

The metals which have been used extensively and which have been shown to cause little or no reaction in the tissues are stainless steel and tantalum. Zirconium* is a similar metal which has recently become available to us for experimental purposes. Bites⁵ working in this laboratory has shown that it causes no more tissue reaction than stainless steel and tantalum when used for suture material or for the repair of cranial defects. We have investigated the reaction of the pleura to zirconium when it has been used as a noncompressible prosthesis.

The plastic in which we have become interested is methyl methacrylate (Lucite) an acrylic resin which has been shown to produce little or no reaction in tissues.^{6,7} Wilson and Baker⁸ have studied its effect on the extrapleural and pleural tissues of laboratory animals and have found only minimal tissue reaction. They have used hollow balls made of this material to fill the extra-

*The zirconium prostheses used in these experiments were furnished by the Foote Mineral Co., Philadelphia, Pa.

pleural cavity following extrapleural pneumonolysis in the treatment of patients with pulmonary tuberculosis.⁷ It would seem that the use of noncompressible balls might be a satisfactory answer to the problems of a material that would fill a cavity of any size and shape.

EXPERIMENTS

Total pneumonectomies were done on dogs. In those in which no prosthesis was used the heart and mediastinum were soon pulled over toward the lateral chest wall thereby producing considerable overdistention of the remaining lung. Fig. 4 shows a dog's chest roentgenogram six weeks after a left pneumonectomy.



Fig. 5.—A dog sacrificed three months following left pneumonectomy without the use of a prosthesis. The overdistention of the right lung is apparent. The left pleural cavity was collapsed. The heart and mediastinum were over against the left side of the chest wall. The lower part of the right lung was over against the left side of the chest wall.

The mediastinum is shifted and the right lung comes over to the left side of the chest wall in the lower part of the thorax. This is more marked than in man because of the dog's thin mediastinum. When such a dog was sacrificed after three months, the right lung was found to be greatly overdistended and the left pleural cavity was found to be empty and collapsed (Fig. 5). The pleural surfaces appeared to be grossly normal. Microscopically the tissues were practically normal (Fig. 10, A).



Fig. 6.—A, Dog four months following left pneumonectomy with the introduction of a zirconium prosthesis. The mediastinum is maintained near the midline, and the right lung is not overdistended. B, When the roentgenogram was taken with the dog in the erect (human) position the prosthesis changed considerably in position.

A zirconium prosthesis was placed in the pleural cavity following pneumonectomy in each of four dogs. The prosthesis was an airtight hollow box 10 by 6 by 3.5 cm. In twelve dogs the pleural cavity following pneumonectomy was filled with one inch hollow balls of methyl methacrylate (Lucite)*. In closing the chest as much air was removed as possible and 100,000 units of penicillin were placed in the pleural cavity. The following day any excess fluid was removed from the pleural cavity by thoracentesis and an additional 100,000 units of penicillin were injected. Thoracentesis was not done thereafter. In no instance did

*The Lucite balls used in these experiments were obtained from the Nichol Product Co. Moorestown, N. J.

infection occur. Three of the sixteen dogs died three weeks or more following operation. In none of these did the pneumonectomy or the presence of the prosthesis appear to be the cause of death. Other dogs were sacrificed at varying intervals to observe the reaction of the pleura.

RESULTS AND COMMENTS

The zirconium prosthesis obviously was not of the size and shape of the pleural cavity but it did occupy space and thereby prevented the shift of the mediastinum and overdistention of the remaining lung (Fig 6 A). The longest interval at which a dog was sacrificed following operation was four months.



Fig 7.—A dog sacrificed four months following left pneumonectomy with the introduction of a zirconium prosthesis. The right lung was not overdistended. The prosthesis was free in the pleural cavity, and there were 600 c.c. of fluid around it. There was moderate inflammatory reaction and thickening of the tissue around the prosthesis.



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The prosthesis lay free in the pleural cavity (Fig 7). There were about 60.0 cc of fluid present. There was a moderate inflammatory reaction of the parietal pleura, with some thickening of the structures surrounding the prosthesis to gross inspection. There was considerable evidence of inflammation on microscopic section (Fig 10, C).

While the zirconium prosthesis caused considerable reaction in the pleura, it was tolerated in the pleural cavity for four months and might well have been tolerated indefinitely. However, a solitary prosthesis made of metal would not be practical because of the difficulty of obtaining the correct size and shape for individual patients. Moreover, if its removal should become necessary because



Fig 3—A dog sacrificed two months after left pneumonectomy and introduction of twenty-four one-inch lucite balls into the pleural cavity. The right lung was not overdistended. There was just enough fluid present to fill the space between the balls (35.0 cc). There was minimal reaction of the pleura.

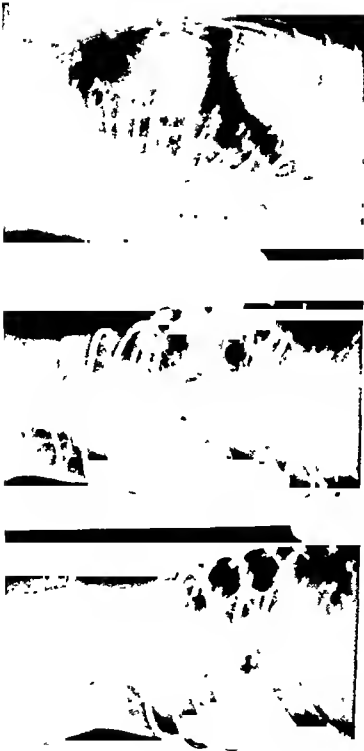


Fig. 8—4 Dog one month after left testicular ectomy and introduction of twenty four inch duct. This is a transverse section. The testis is in the center of the duct. A large view of the testis is in the center of the duct. A large view of the testis is in the center of the duct.

of infection this could not be accomplished through a small drainage opening. The weight of the zirconium prosthesis would also be a problem as the prosthesis changed considerably in position as the dog changed from the prone to the erect position (Fig 6). Perhaps the motion in part may have been responsible for the irritation of the pleura.

When the hollow balls of methyl methacrylate were used as the prosthesis they distributed themselves evenly throughout the pleural cavity and effectively prevented mediastinal shift and overdistention of the remaining lung (Fig 8 A, B, and C). To date the longest interval following operation that one of these dogs has been sacrificed is two months. The balls were free in the pleural cavity (Fig 9). There was no more fluid than was necessary to occupy the space between the balls (35 cc). There was minimal reaction of the pleura. This was considerably less than with zirconium and consisted chiefly of fibroblastic proliferation with minimal round cell infiltration in some areas (Fig 10 A, B and C).

These dogs have not been studied long enough so that this must of necessity be a preliminary report. Nevertheless our observations to date indicate that there has been a minimal reaction of the pleura to methyl methacrylate balls and that these balls are effective as a prosthesis in the pleural cavity in preventing mediastinal shift. These observations in addition to those of Wilson and Baker⁶ who used similar material in the extrapleural cavities strongly suggest that this material will prove to be a satisfactory prosthesis for use in the pleural cavity of man to prevent overdistention of the remaining lung following pneumonectomy. The use of multiple balls would seem to be the ideal way of dealing with pleural cavities of various sizes and shapes.

SUMMARY

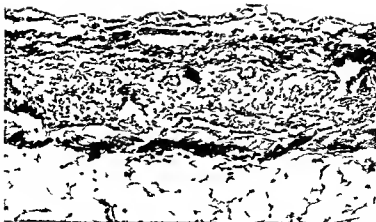
1 Clinical experience and the experimental work of Cournand and his associates indicate that it would be desirable to prevent mediastinal shift following pneumonectomy and thus avoid overdistention of the remaining lung. This can be accomplished by an extensive thoracoplasty. In the presence of infection the thoracoplasty must be done. In the absence of infection it is desirable to have some method less extensive than a thoracoplasty whereby overdistention of the remaining lung can be prevented.

2 It is suggested that a noncompressible prosthesis may be introduced into the pleural cavity at the time of pneumonectomy as a means of preventing post operative mediastinal shift and overdistention of the remaining lung.

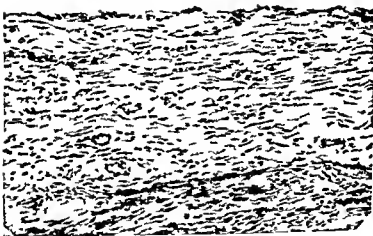
3 Two types of prostheses have been studied in the dog: (a) a solitary large hollow metal prosthesis of zirconium and (b) multiple small hollow plastic balls of methyl methacrylate (Lucite).

Fig 10—Micro monectomy when no

A Three months after pneumonectomy grossly normal. Microscopically, three months after pneumonectomy, considerable thickening of the pleura with inflammatory reaction with infiltration of leukocytes. B Six months after pneumonectomy, grossly normal. Microscopically, there was minimal thickening of the pleura with some edema and fibroblastic proliferation in some areas. (X130)



A.



B.



C.

Fig 10 (For legend see oppos to page)

THE USE OF THE JEJUNUM IN THE CONSTRUCTION OF AN ANTETHORACIC ESOPHAGUS

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THE perfection of transthoracic gastroesophagostomy, a procedure used following the resection of the lower half of the esophagus, has provided many patients afflicted with obstructive lesions in the esophagus with a satisfactory passage of food into the stomach. This operation may be accomplished even in those instances when the esophageal lesion is situated rather high in the esophagus. In certain cases of carcinoma of the esophagus gastroesophagostomy has given excellent results as reported by Garlock,¹ ² Phemister,³ and others. However there are instances in which the lesion is situated so high in the esophagus that the stomach cannot be brought up into the chest to accomplish a safe anastomosis with the upper esophageal segment. This intrathoracic anastomosis may also be undesirable in certain cases of acquired strictures of the esophagus. Since total esophagectomy is a shorter surgical procedure than a gastroesophagostomy the condition of the patient during operation may force the surgeon to select the shorter procedure. It therefore appears that a number of conditions may arise necessitating the construction of an antethoracic esophagus.

Our previous experiences with the use of skin transplants for the construction of an artificial esophagus convinced us that such a procedure was lengthy and almost never free of fistulous formation. The lumen of such skin tubes often became obstructed because of stenosis and the growth of hair on the inside of the tube.

Our first opportunity to use the jejunum in the construction of an antethoracic esophagus came in 1940. This occurred in connection with a patient, a man 46 years of age, who presented a typical history of esophageal obstruction. Esophagoscopy and biopsy revealed a squamous cell carcinoma of the esophagus. At operation performed in November 1939 the entire thoracic esophagus was removed. The operation was terminated by a cervical esophagostomy and a gastrostomy for feeding. One year later (1940) a segment of jejunum was used to construct an antethoracic esophagus. While the patient was being prepared for the second stage of this operation early signs of cord paralysis were discovered and further operative procedures were abandoned. However this experience led us to believe that the jejunum could be used satisfactorily for the construction of an external esophagus.

During the past six years we were unable to do the transthoracic gastroesophagostomy on two patients because the stomach could not be brought sufficiently high up into the chest to accomplish a safe anastomosis. Seven transthoracic anastomoses were performed with good results in six cases. One

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Fig. 1—A roentgenogram showing an extensive carcinoma of the upper third of the thoracic esophagus



Fig. 2—The jejunum is anastomosed to the stomach and brought up through a subcutaneous channel. The serosa and muscularis of the upper one half of the bowel were stripped off. This photograph was taken two weeks after the operation. One catheter is in the esophageal opening the other in the stripped jejunum. A necrosis occurred.

patient died from a gastric fistula which developed from devascularization of the lesser curvature of the pylorus. Nevertheless, this operation is superior to one necessitating the construction of an antethoracic esophagus.

The jejunum was utilized in the following manner. After total thoracic esophagectomy, the patient is left with a cervical or infraclavicular esophagostomy and a gastrostomy for feeding. At least two weeks after operation, the abdomen is opened and a convenient loop of the upper jejunum is isolated with its blood supply preserved. The lower end is anastomosed to the stomach and the continuity of the bowel is reestablished by lateral or end-to-end anastomosis. The isolated segment of jejunum measuring approximately 50 cm in length is stretched as much as its mesenteric blood vessels will allow. Certain of the mesenteric vessels supplying the proximal half of the jejunal segment must be cut in order to overcome the natural coiling of the bowel and thus increase its length. This segment is then pushed upward through a subcutaneous tunnel in the anterior thoracic wall. The upper open end of the bowel is brought out through a buttonhole incision in the skin adjacent to the esophageal opening. These two ends may be anastomosed later, thus completing the procedure.

In the development of this operation, it occurred to one of us that in order to extend the length of the coiled piece of jejunum the following technique could be employed. We removed the serosa and the muscularis over the upper one half of the jejunal segment leaving essentially a mucosal lined tube. This maneuver lengthened the stripped portion of the jejunum and destroyed its blood supply. The lower half of the bowel remained intact. We reasoned that if a segment of bowel was made sufficiently thin it would have a better chance to "take" as a devascularized transplant.

The first time we tried this new method excellent healing occurred so that within two weeks we had a mucosal lined tube communicating with the stomach and ready for an anastomosis with the esophagus. However, the lumen of this tube was found to be rather narrow in the region where the serosa and muscularis were stripped and thus devascularized. This particular segment of the jejunum continued to constrict until only a small catheter could be passed into the lumen, thus too small for the swallowing of food. The difficulty was overcome by placing a split thickness skin graft made into a tube into the subcutaneous bed under the constricted segment of jejunum. The final results were entirely satisfactory. Similar stenosis of lumen occurred when the jejunum was left intact except for the necessary destruction of the blood supply in its upper half. Stenosis occurred only in the part of the transplanted jejunum where the blood supply was deficient.

The consideration of these results, those of Yudin,⁴ Ladd and Swenson,⁵ and others made it desirable to repeat these operations on animals in order to understand more fully the minor defects encountered by us. Experiments were devised to answer the query as to whether the residence of a segment of bowel in the subcutaneous tissue contributed to the atrophy of the lumen or whether this atrophy was entirely the expression of lack of blood supply.

In the first experiment, using several dogs, a segment of jejunum measuring approximately 20 cm was dislocated into the subcutaneous tissue. The



Fig. 6—*a*, *b*, and *c*. Three specimens of subcutaneous jejunum two to three weeks after the mesenteric blood supply was interrupted in the second stage. The cross sections show the lumen to be normal.

open ends of the bowel were brought out through buttonhole incisions into the skin. The mesenteric blood supply was left intact. The continuity of the bowel was re-established by either end to end or lateral anastomoses. Two to



Fig. 3



Fig. 4

Fig. 3—It enters area of a far advanced carcinoma of the esophagus adherent to the aorta and extending up as its arch.

Fig. 4—The jejunum is anastomosed to the stomach and brought up subcutaneously to meet the esophagus. Note the pouch to the left of the umbilicus where the jejunum is coiled. The small fistulous opening indicates the point of anastomosis.

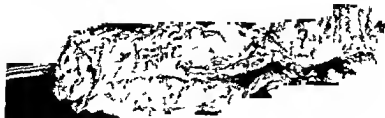


Fig. 5—A specimen of jejunum removed from the subcutaneous tissue after the mesenteric blood supply was interrupted at a mesocol stage. The lumen of the bowel is a ligulate

left auricle because of its posterior position. Often twisting and rotating the heart in order to obtain sufficient exposure to suture the defect results in interference with the blood flow at the base of the heart with consequent cardiac embarrassment. Most important is the thin walled, friable musculature, which not only gives no support in closing the wound, but which also makes suture very arduous. The stitches readily pull out and it is difficult to confine them to the substance of the muscle and not enter the chamber where damage to the intima predisposes to clot formation which could prove fatal. Furthermore, it is even a task to control the hemorrhage temporarily by digital pressure while sutures are being placed since there is little to push against. This plus the combination of a rapidly beating heart and the great rapidity of the hemorrhage (much greater than in the ventricles although under less pressure) all contribute to the dilemma of the surgeon. However the placing of a stay suture through the apex of the heart as advocated by Beck,¹² the application of the Sauerblich method¹⁴⁻¹⁴ for temporary arrest of the circulation and the use of the Trendelenburg artery clamp¹⁵ for temporary control of the bleeding are all well tried methods which the surgeon can resort to in solving the particular problem at hand.

Observations on the absorbability¹⁶⁻¹⁷ and hemostatic action¹⁸⁻²⁰ of the gelatin sponge in controlling hemorrhage from wounds experimentally produced in the liver,²¹⁻²² great vessels²³ and cardiac ventricles²⁴⁻²⁵ of dogs led us to study the feasibility of using this agent in wounds of the cardiac auricles.

EXPERIMENTS

Experiments were performed on eighteen dogs ranging from 5 to 14 kg in weight, using ether anesthesia and the intratracheal positive pressure apparatus, maintaining a constant pressure of between 30 and 40 mm. of Hg during the operative procedures. Aseptic precautions were observed throughout. Muscle splitting incisions were used and the chest was entered through the fourth and fifth interspaces on either side. Sufficient exposure was obtained by the use of self retaining retractors and it was unnecessary to resect a rib. The lungs were retracted and the pericardium opened parallel with and just anterior or posterior to the phrenic nerve. There were no cases of ventricular fibrillation even though procaine solution was not used.

Hemorrhage of great magnitude was produced by removing about 1 cm. of the tip of the auricular appendage (see Fig. 1), or by thrusting the scalpel into the auricular wall at the base of the appendage. Bleeding in most instances was diametric. Hemorrhage from wounds of the appendage could be temporarily controlled by opposing the cut edges by means of loosely applied hemostats. Bleeding from wounds in the auricular wall proper, however, was more difficult to arrest and had to be done by digital pressure.

Dry compressed gelatin sponge cut to conform with the size of the wound was placed over the bleeding surface and held there with firm finger pressure for approximately ten minutes, at which time the hemorrhage had usually ceased (see Fig. 2). In several cases it was necessary to apply a second or a third sponge before hemostasis was accomplished.

CONTROL OF HEMORRHAGE FROM THE CARDIAC VESSELS BY THE GELATIN SPONGE

AN EXPERIMENTAL STUDY

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REHN¹ in Germany in 1896 performed the first successful cardiorrhaphy. Since then reports of successful suture of wounds of both the cardiac ventricles and auricles²⁻⁴ have appeared in the literature with increasing frequency so that now cardiorrhaphy has become a standard emergency procedure when the surgeon is confronted with evidence of increasing cardiac tamponade. Nevertheless the incidence of heart wounds in civilian practice remains relatively small and in 1936 Bunker⁵ reported their incidence in only 0.1 per cent of all the surgical patients admitted to the Medical College of Virginia Hospitals. And in the same year Elkin⁶ reported that in only 2 per cent of all the penetrating wounds of the chest were there associated wounds of the heart.

However, this is slightly misleading, as many persons die of stab wounds in the precordium inflicted by a knife, ice pick or bullet who never come under the observation of a physician. Particularly is this true of wounds of the auricles which comprise roughly only 10 per cent of all cardiac wounds, probably because of their posterior position. The walls of these chambers, unlike the thick ventricular musculature, offer little resistance to the escape of blood.

That auricular wounds are of a more serious nature than those of the ventricles was recognized by Rehn and may be seen in a comparison of the mortality figures. Because of more meticulous asepsis, improved operative technique, and the administration of intravenous fluids preoperatively to increase the blood volume and hence increase the cardiac output, Elkin⁶ in his series of sixty-one cases reported a decrease in the mortality rate in wounds of all four cardiac chambers, the right and the pulmonary artery from 42 per cent in 1941 to 22 per cent in 1944. During this same period and in this same group of cases three auricles were injured with one death on the operating table, a mortality of 33 per cent. In a series of forty-two wounds of the heart reported by Griswold and Wigmore⁷ in 1942 four were in the auricles. Of these four three patients did not recover, making a mortality of 75 per cent. Likewise in 1944 Under and Hodes⁸ reported three deaths and three recoveries from wounds of the auricles (50 per cent mortality) in a study of twenty-seven traumatically injured hearts.

A combination of factors exist to account for the high mortality in auricular wounds. First is the difficulty in approaching these structures, particularly the

brought the hemorrhage under control. This was accomplished in the other case by suture of the muscular wall at the base of the appendage after considerable difficulty due to the friability of the musculature. In one control case hemorrhage was stopped by a ligature at the base of the appendage without using the gelatin sponge.

The pericardium was closed with continuous silk sutures leaving a small portion at one end open for drainage. Two pericostal linen sutures approximated the ribs and the muscles and fascia were closed in layers with silk. The lungs were inflated just before placing the last suture in closing the chest wall to obviate a pneumothorax. Intercutaneous stitches and collodion dressings were applied to prevent the dogs from pulling at the sutures.



Fig. 2.—Showing control of hemorrhage from wound of aorta by application of gelatin sponge.

Because the sponge adhered almost as readily to the gloved surface as to the bleeding surface even when the former was smeared with blood before the application of digital pressure in our later experiments collophane and finally perforated Calkloid were placed between the sponge and the glove. The Calkloid proved excellent. It does not stick to the glove and any tendency to adhere to the sponge can be overcome by a few drops of saline solution which penetrate the perforations and render the Calkloid easily removable. This can be accomplished even when the Calkloid has been made to adhere to the sponge by a 2 per cent solution of achrom prior to operation so as to facilitate handling the two substances.

In two days the bleeding was so profuse that it could not be controlled by the sponge. In one of these a ligature encircling the base of the appendage



Fig. 1—Showing hemorrhage from wound of auricle

RESULTS

All eighteen dogs survived the operative procedure and were sacrificed or died from three hours to seventy seven days postoperatively (see Table I and Figs 3-4-5 and 6). There was no secondary hemorrhage in any instance. Of nine dogs with wounds of the left auricular appendage seven were sacrificed at from seven to seventy seven days. One died three hours postoperatively of a pneumothorax and another after one day the cause of death in this case being undetermined. One dog with a wound of the right auricular appendage was sacrificed at fourteen days and two others with stab wounds of the left auricular



Fig 3-4 showing specimen of heart one day after application of gelatin sponge for control of hemorrhage from wound of auricle

will were sacrificed at twenty eight and thirty five days. Finally of five dogs in whom wounds were made in the right auricular wall three were sacrificed at seven fourteen and twenty eight days respectively while one died of general sepsis and purulent pericarditis after two days and one of distemper three days postoperatively.

At autopsy there were usually adhesions between the chest wall lungs and pericardium on the operative side. Adhesions were also present within the pericardial sac in our earlier experiments but with improvement in operative technique adhesions within the pericardial sac were confined to the region of

TABLE I

DOGS NO	DATE OF OPERATION	SITE OF WOUND	DAYS LIVE	CAUSE OF DEATH	ALTOPHY
612	5/20/46	Left auricular apponage	10	Sacrificed	Few adhesions within pericardial sac, sponge in place, no secondary hemorrhage
116	9/14/46	Left auricular apponage	77	Sacrificed	Many adhesions in chest and pericardial cavity, auricular apponage contracted and defect sealed, no gross evidence of sponge no secondary hemorrhage
145	4/15/46	Left auricular apponage	29	Sacrificed	Few adhesions, sponge still evident defect sealed, no secondary hemorrhage
150	9/19/46	Left auricular apponage	1	Died (?)	Sponge strongly adherent to auricular wall, no secondary hemorrhage
427	8/20/46	Left auricular apponage	2	Sacrificed	Many adhesions of lung to the chest wall and mediastinum also many within pericardial sac, sponge partly absorbed, no secondary hemorrhage
155	8/27/46	Right auricular apponage	14	Sacrificed	No adhesions, sponge still present wound defect, no secondary hemorrhage
812	9/24/46	Left auricular apponage	3 hr	Defect surgically	Sponge adherent to aortic, no secondary hemorrhage
420	9/24/46	Left auricular apponage	53	Sacrificed	Only few adhesions of heart to pericardium site of wound noted by suture stitches only, sutures identified no secondary hemorrhage
157	8/30/46	Left auricular apponage	76	Sacrificed	Heart outside of pericardium (not closed at operation), dense adhesions around site of left auricle sutures identified, no secondary hemorrhage
160	9/4/46	Left auricular apponage	7	Sacrificed	Only few adhesions, sponge readily identified, sealing wound, no secondary hemorrhage
346	12/13/46	Left auricular wall	30	Sacrificed	No adhesions, no evidence of sponge, fibrous tissue present over site of wound, no secondary hemorrhage
351	12/23/46	Right auricular wall	14	Sacrificed	Moderate adhesions within pericardial sac, sutures identified, tissue thick ened about sutures, no secondary hemorrhage
620	1/2/47	Right auricular wall	24	Sacrificed	Thick adhesions over sponge, latter still present—pale yellow gelatinous, and strongly adherent, no thrombus on endocardium at site of wound, no secondary hemorrhage
119	1/7/47	Left auricular wall	21	Sacrificed	Adhesions over sponge only, endo- cardium wound well healed, no secondary hemorrhage
643	1/8/47	Right auricular wall	14	Sacrificed	No adhesions within pericardial sac except over sponge, wound in endo- cardium barely visible, no secondary hemorrhage
647	1/9/47	Right auricular wall	2	Died of sepsis and pericarditis	Per sanguineous fluid in each chest sternotomy, pericarditis into cardium almost white, no secondary hemorrhage
623	1/14/47	Right auricular wall	3	Died of dis- tension	Both lungs hemorrhagic and a whitish pericardial sac normal sponge appeared yellow and adherent to right auricle, no secondary hemorrhage
123	1/22/47	Left auricular wall	7	Sacrificed	Dense adhesions over sponge only in fraction of right ventricular wall, large thrombus in right ventricle emerged in the tricuspid foramen encompassed endocardium & right auricle in vicinity of wound ap- peared bruised and with mural thrombus, no secondary hemorrhage

especially in controlling bleeding of any magnitude. Much of this comes from personal experience and the following points are intended only as a guide. First, the sponge should be compressed between the fingers to a thickness of roughly one sixteenth inch before application to the bleeding surface. Second, it cannot merely be placed against the bleeding point but rather must be held there with firm digital pressure for a matter of minutes until it becomes adherent. In the case of an auricular wound this is approximately ten minutes. Third, and probably the most important single factor, is to prevent the sponge from sticking to the rubber glove, as nothing is more discouraging than to have the hemorrhage under control and then find the sponge strongly adherent to the finger. This in our experience was most successfully combated by the use of perforated

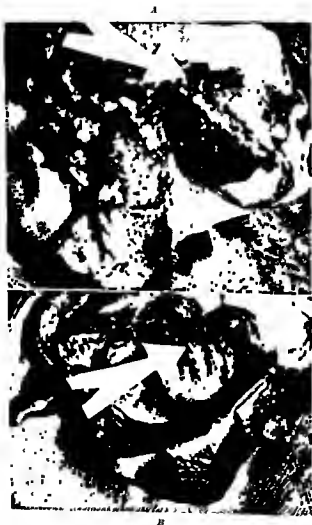


Fig 5—Showing specimen of heart after twenty-one days. A, Gelatin sponge firmly adherent to wall of auricle overlying wound. B, leaked wound in endocardium of auricle.

the sponge. Autopsy on the four dogs which died revealed the gelatin sponge to be firmly adherent to the wound with no evidence of secondary hemorrhage. Autopsy on the fourteen who were sacrificed showed no infection, hemorrhage, fluid, or aneurysm formation, and the endocardium at the site of the wound appeared off white in color and smooth and glistening, with two exceptions. One dog with a wound of the right auricular wall which was sacrificed after twenty-eight days had a small mural thrombus 2 mm in diameter strongly attached to the endocardium where it was pierced by the scalpel. Another which underwent the same procedure and was sacrificed after seven days revealed at autopsy an area of infarction at the apex of the right ventricle. A large thrombus was



FIG. 4.—Showing specimen of heart after seven days with gelatin sponge sealing off wound of auricle.

also present within the lumen of the right ventricle enmeshed in the chordae tendineae of the tricuspid valve. The endocardium of the right auricle in the vicinity of the wound appeared bowed and a 5 mm flat mural thrombus was present. The sponge was adherent to the epicardium in all cases and was absorbed in from five to eight weeks. The site of the wound in those cases which silk sutures and ligatures were used in controlling the hemorrhage was marked in varying degrees of fibrosis.

COMMENT

Certain points in the technique of applying the gelatin sponge must be mastered. Its proper use can mean the difference between success and failure,



Fig. 6.—Showing suture on left after twenty-eight days with gelatin sponge becoming the (suture) in wall of auricle overlying wound.

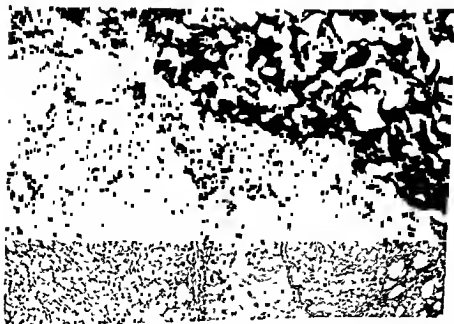


Fig. 7.—Showing gelatin sponge patch covering wound of auricle after seven days. There is active fibroplasia which has filled in the defect in the wall of the auricle.

CONGENITAL ARTERIOVENOUS FISTULA BETWEEN THE INTERNAL MAXILLARY ARTERY AND PTERYGOID PLEXUS

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(From the Department of Surgery Stanford University School of Medicine)

ABNORMAL communications between arteries and veins occurring at birth or becoming evident in childhood or adolescence, have formed the basis for a number of stimulating papers. In 1918, Halsted³ presented a case of congenital arteriovenous fistula of the neck at a meeting of the American Surgical Association and mentioned at the time that congenital fistulas occurring without nevi were extremely rare. Callander⁴ in 1920 collected all the cases of acquired and congenital fistulas that had been reported up to that time and found that there were only 2 without nevi in 447 fistulas of all varieties while with nevi the condition was reported in only 6 instances. That this is not a true indication of the frequency of these interesting lesions has been emphasized for undoubtedly there are many unreported cases. In 1924 Rienhoff⁵ published a paper in which the literature on congenital arteriovenous fistulas was reviewed and the Johns Hopkins Hospital cases were presented in detail. In 1925 Reid^{10, 12} published several papers in which acquired and congenital fistulas were discussed comprehensively. Various other authors notably Lewis¹³ Elkin¹⁴ Pemberton and Saint¹⁵ and Ward and Horton¹⁶ have reported individual or small series of cases. There are quite a number of congenital vascular lesions of the extremities in the literature at the present time some of which were reported by these authors but they are not included in this study.

Observations by Sabin^{17, 18} and Woollaid¹⁹ indicate that congenital arteriovenous fistulas are due to a persistence of embryologic vascular channels. Arteries and veins arise from a common capillary plexus affording an explanation for the occurrence of abnormal communications. In discussing this Reid aptly expressed wonder that the abnormal occurrence is so infrequent.

Some confusion exists in the terminology applied to congenital vascular lesions which at times makes it difficult to identify positively the anomalies as to type. This was particularly true in the early literature. Since 1900 most of the congenital vascular tumors with communications between arteries and veins have been called arteriovenous aneurysms which probably is the best descriptive term in use since it correctly implies that there is dilatation in the involved vessels. It is possible that some of the early cases included in this study may not have had communications between arteries and veins but they are included because it seemed most likely that they did exist. The reason for casting any doubt lies in the variation in terminology used in the failure to report whether a continuous murmur was heard over the tumor or in not stating if arterial blood was seen in veins.²⁰

arteries, two by multiple ligations and coagulation, and one by simple ligation of veins. Twelve of the twenty-two cases required more than one operation to relieve the symptoms either partially or totally.

The following is a case report of a congenital arteriovenous fistula between the internal maxillary artery and pterygoid plexus.

CASE 1 (History No 20701)—D. K. was a 6-year-old girl who was brought to the clinic by her stepmother with the complaint of a pulsating swelling below the left ear. The stepmother had noticed the pulsation in 1944, when the child came under her care. The patient stated that she had heard a buzzing in the left ear for as long as she could remember. A tonsillectomy and adenoidectomy six months previously was attended by mild postoperative hemorrhage. There was no history of any injury which might have caused an arteriovenous fistula. The child lived easily, but had only moderate dyspnea on great exertion. The stepmother stated that she was a rather nervous child, being somewhat difficult to manage at times.



Fig 1—Photograph showing enlargement of the left side of the face before operation.

Physical examination revealed a well-developed and nourished girl. The left side of the face was larger than the right (Fig 1). Below the lobe of the left ear there was a visible pulsation, essentially a dilated and pulsating external jugular vein. A pronounced thrill could be felt over the left side of the face maximal in front of the ear. There was a continuous loud murmur with systolic accentuation, heard maximally in front of the left ear, but transmitted over the cranium and down the vessels in the neck. The murmur could be diminished by pressure over the left common carotid but pressure over both common carotids was required to obliterate it. Examination of the heart revealed a soft systolic murmur along the left sternal border. The blood pressure in both arms averaged 115/60. Laboratory examinations revealed negative blood Wassermann and Hinton flocculation tests, normal blood count and a negative urinalysis. The electrocardiogram was normal. Roentgenogram of the skull and face showed that the left half of the mandible was larger than the right (Fig 2). Roentgenograms of the chest taken five days before operation showed a heart shadow 9.5 cm in transverse diameter. Eight days after obliteration of the fistula it measured 8.7 cm (Fig 3).

Congenital arteriovenous fistulas exhibit the same
produce
large

in a con
known as Branham's head, cardiac phenomenon since his description of it in an
acquired fistula in 1890. However, when numerous communications exist, pre-
cluding complete occlusion of all the fistulas, this phenomenon is not demon-
strable. Cardiac enlargement occurs if the communications are large, and after
obliteration of the fistula the heart size has been observed to return to normal.
This effect was not recorded by Dandy in cerebral arteriovenous fistulas nor has
it been seen in many of the cranial types with multiple small openings between
the arteries and veins. Proximal dilatation of the principal artery or arteries
supplying the fistula has been found in many congenital fistulas and dilation
of the communicating veins is a common observation.

The increased vascularity of the tissues near an arteriovenous fistula is re-
sponsible for various local effects. One of the most striking is the stimulation
to the growth of the long bones. In our case an increased growth of the mandible
was observed. Increased surface temperature is present near the lesion due to
the richness of the arterial blood supply.

In reading the case reports on congenital arteriovenous fistulas of the face
and neck one is struck by the heroic attempts that have been made to cure these
lesions, and how frequently success has been only partial. As might be expected,
cure is not certain unless the arterial communications are either ligated, extirpated
or thrombosed. Frequently the exact location of the fistulas has not been dem-
onstrated before or, in fact, during operation. Of the twenty-three treated pa-
tients reported in the literature (Table I), only thirteen were cured by surgical
means. In six instances a direct attack on the involved vessels with excision was
successful. Four patients were cured by ligation and division of multiple
small fistulas. Only one of the cures was effected by ligation of the principal
artery leading toward the involved vessels. Kent and McGuire²² reported a cured
case of congenital fistula between the external carotid artery and the external
jugular vein in which the artery and vein were ligated and transected, the prox-
imal vein then being twisted to occlude the fistula. Ferris Smith²³ reported a
cured case of aneurysm in the tympanum in which he ligated the veins and
packed the aneurysm. Improvement in the amount of pulsation and other symp-
toms followed similar surgical measures in ten cases. In this group five were
benefited by multiple ligations and excisions, two by the ligation of the principal

TABLE I. RESULTS OF TREATMENT IN TWENTY-THREE CONGENITAL ARTERIOVENOUS FISTULAS
OF THE FACE AND NECK

	CURED	IMPROVED
1	6	3
1	4	3
1	1	1
Ligation of principal veins and packing of aneurysm	1	3
Ligation of principal veins		
Ligation of principal arteries and twisting of involved vein	1	

It was decided that localization of the site of the fistula by angiography would be helpful. Accordingly, on Nov. 14, 1946, under general anesthesia the left common carotid was exposed through a short transverse incision and 10 cc of thorotrast were injected into it while stereograms of the skull were rapidly taken (fig 4). The roentgenograms showed that the opaque medium went directly into the external carotid artery, avoiding the internal carotid, and then into the internal maxillary artery. Here abnormal arteriovenous communications between the internal maxillary artery and veins of the pterygoid plexus could be seen. The thorotrast could then be followed down a large vein running toward the base of the neck. It was interesting to note that neither the internal carotid nor the branches of the external carotid were visualized indicating how great the urge is for blood to rush toward a fistula. There were no ill effects from this procedure and the wound healed per primam.

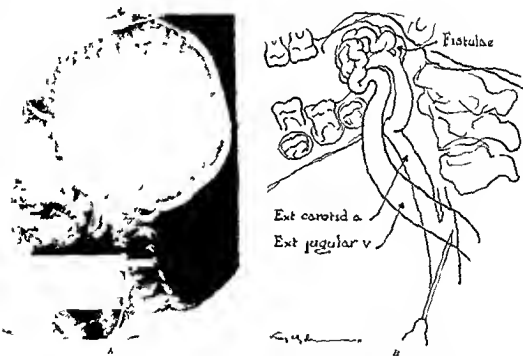


FIG 4—A Thorotrast carotid angiogram. B Tracing of the angiogram showing the location of the internal carotid and branches of the external carotid. Note also the dilatation of the external carotid artery and external jugular vein.

Various methods of treating this communication were considered. A direct attack on the fistula would have entailed a bloody and disfiguring procedure. Inasmuch as it required compression of both common carotids to stop the murmur, it was obvious that some of the blood supply to the fistula was coming from the opposite side. Therefore simple proximal ligation of the external carotid artery would have been attended by the possibility of incomplete obliteration. It was decided to attempt to pack the artery with muscle at the site of the fistula and thus directly occlude the abnormal communications (as performed by Brooks¹² for pulsating exophthalmos secondary to carotid cavernous sinus arteriovenous fistula).



Fig. 2—Roentgenogram showing enlargement of the left half of the mandible. The measurements are in millimeters.

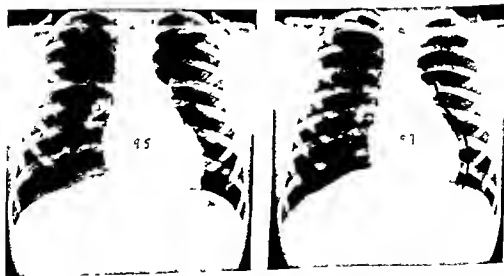


Fig. 3. A Preoperative roentgenogram of the heart shadow showing a transverse diameter of 9.5 cm. B Eight days after obliteration of the fistula the heart shadow measured 8.7 cm. the heavy line is a tracing of the left border of the heart taken from the preoperative film.

It was decided that localization of the site of the fistula by angiography would be helpful. Accordingly, on Nov 14, 1946, under general anesthesia, the left common carotid was exposed through a short transverse incision and 10 cc of thorotrast were injected into it while stereograms of the skull were rapidly taken (Fig 4). The roentgenograms showed that the opaque medium went directly into the external carotid artery, avoiding the internal carotid, and then into the internal maxillary artery. Here abnormal arteriovenous communications between the internal maxillary artery and veins of the pterygoid plexus could be seen. The thorotrast could then be followed down a large vein running toward the base of the neck. It was interesting to note that neither the internal carotid nor the branches of the external carotid were visualized indicating how great the urge is for blood to rush toward a fistula. There were no ill effects from this procedure and the wound healed per primam.

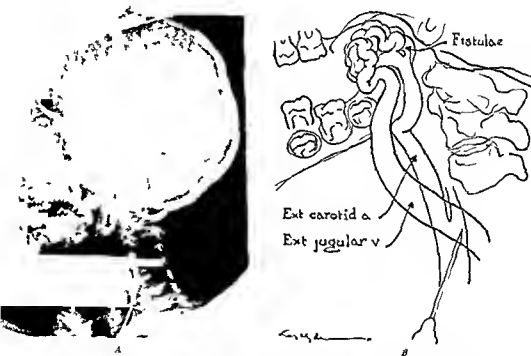


Fig 4—A Thorotrast carotid angiogram. B Tracing of the angiogram showing the dye outfitting the internal carotid and branches of the external carotid. Note also the dilatation of the external carotid artery and external jugular vein.

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At operation Nov. 19, 1940, under ether anesthesia, a transverse incision was made in a normal skin fold, just beneath the left mandible. After the platysma was incised a very large pulsating external jugular vein was encountered (Fig. 5). This vessel was freed loosely ligated with medium silk, and transected, thereby allowing better access to the carotid sheath. The common, external and internal carotids were identified and freed from their investments. It was noted that the internal jugular vein was a very small almost vestigial structure. The external carotid artery was larger than the internal carotid clearly showing the often described preaxial bifurcation of the artery supplying a fistula. The branches of the external carotid proximal to the fistula namely the superior thyroid, lingual, external maxillary, sternocleidomastoid, occipital and posterior auricular were doubly ligated with medium

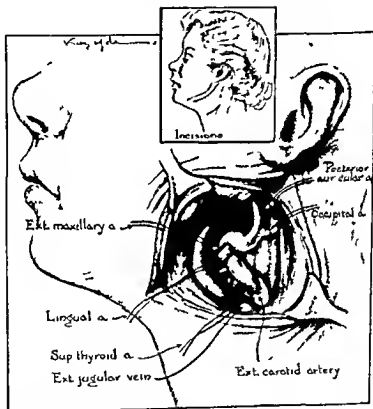


Fig. 5.—Showing the dilated and tortuous external carotid artery and the large anomalous external jugular vein.

Insert.—Showing the skin incisions. They were placed in normal skin folds and the lower incision was used for the carotid angiogram.

silk and transected. When the external carotid was then drawn down from beneath the mandible a plexus of veins could be seen anastomosing the artery. Two bulldog arterial clamps were placed on the artery, one at the bifurcation the other as high as possible next to the mandible. A small transverse incision

the

inset

small

carotid —

he felt within all of the exposed external carotid artery.

with silk just beyond the bifurcation and transected beyond the ligatures. No retrograde bleeding occurred from the open distal end. A bayonet forceps was used to further advance the muscle toward the fistula. The distal end was then ligated with medium silk and a portion excised (Fig 7). Observers noted that the bruit was no longer audible. The wound was closed with interrupted silk sutures, and a surgical dressing was applied.

The child withstood the operation quite well and was returned to bed in good condition. The blood pressure a few hours after the operation averaged 134/88. The wound healed per primam, and there were no postoperative complications. She was discharged from the hospital on the eighth postoperative day and has since been followed in the outpatient clinic. One month after the operation examination revealed that the bruit was not present and the child was quite normal in every respect. The blood pressure at this time was 124/80. Two and one half months after operation a faint bruit could be heard just in front of the left ear. Pressure over the right external carotid stopped the murmur, indicating that this vessel is now supplying a small opening not occluded by the muscle. She is not conscious of the murmur. The stepmother states that the child is less nervous than previously, and is easier to manage.

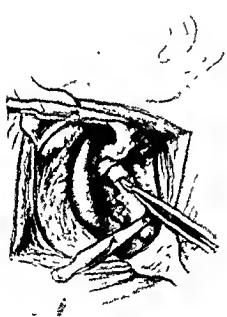


FIG 6



FIG 7

Fig 6—Method of inserting the muscle strip. The incision in the external carotid was closed with arterial silk which engaged the proximal end of the muscle. The two bulldog clamps were then removed allowing the arterial flow to carry the muscle into the area of the fistulas.

Fig 7—Condition of vessels at close of the operation. The muscle pack was further advanced through the open distal end of the artery. A segment of the artery was then excised. The arteries were doubly ligated and transected.

SUMMARY

1 The reported cases of congenital arteriovenous aneurysms of the face and neck are briefly reviewed, illustrating their close resemblance to acquired fistulas.

Name	Sex	Arteriovenous aneurysm	Site	Large pulsating tumor or swelling, dilated internal jugular vein, bruit	Ligation of common carotid artery and external jugular vein, no carotid bruit	Ligation of common carotid artery and external jugular vein, no carotid bruit	Greatly improved, lumps cured	Common carotid enlarged
1901, Eklund	30, F	Arteriovenous aneurysm	Right side of neck	Large pulsating tumor in neck, dysphagia, pulsating throbbing noise, hoarse voice, marked thrill and bruit	Ligation of veins including one large vein going into thorax, ligation of superior thyroid, lingual and facial arteries, excision of large mass of vein etc.	Cured	Atrial communications not demonstrated	Atrial communications not demonstrated
1919, Hjalsted	31, F	Arteriovenous fistulas	Right upper neck	Throbbing swelling of right side of neck, thrill and bruit	1st oper. Dilated ligation and excision of dilated veins, ligation of external carotid 2nd oper. Reind. excision of another communication between an aberrant artery and vein behind parotid	Improved	Brut	Brut
1924, Steinhoff	20, M	Arteriovenous fistulas	Left upper neck	Pulsating, rumbling mass, hyperaesthesia on exercise, marked thrill and bruit, developed with pressure over common carotid	Ligation and transection of eight fistulas between external carotid and external jugular vein	Cured	Absent	Internal jugular vein
1925, Heller	18, M	Arteriovenous aneurysm	Right lower neck	Swelling, pulsing, some asymmetrical face thrill, and bruit	1st oper. Reind. ligation of external jugular vein and transverse colic artery, excision of mass of vessels 2nd oper. Reind. excision of clasp, ligation of internal jugular vein, subclavian artery and vein, thyroid axils	Improved	Fistula was between	subclavian artery and aneurysmal mass
1928, Robertson and Samt	41, F	Arteriovenous aneurysm	Left side of chin and submental region	Swelling on chin, pulsation, thrill	1st oper. Ligation of external carotid 2nd oper. Ligation of right external carotid 3rd oper. Dissection and ligation of veins 4th oper. Dissection and excision of small veins	Improved	Returned six months after 4th operation	with slight fulgences and slight thrill, radium treatment advised

TABLE II—CONT'D

DATE AND AUTHOR	AGE AND SEX	TYPE	LOCATION	PREVIOUS SYMPTOMS	ANALYSIS	DIAGNOSIS	OPERATION	RESULT	COMMENT
1928, Pandafor and Sabin	21, F	Arteriovenous anastomosis	Rt occipital and temporal and regions	Bilateral and pulsating veins; hard front and marked thrill		1st oper., ligation of ex- ternal carotid and ex- cision of veins 2nd oper., excision of ear and vessels	Improved		1st op. 2½ months after 2nd operation from brain hyperemia
1928, Foster and Smith	19, F	Arteriovenous anastomosis	Rt eyelid	Prominent right eye, di- lated veins, thrill and lump over veins		Ligation of right external carotid	Cured		
1929, Smith	31, F	Arteriovenous histula	Tympanum	Pulsating noise in ear, hemorrhage from ear		Ligation of veins and two operations	Cured		Excision of tumor of au- ditory canal and anal le ring
1930, Lewand	26, F	Arteriovenous aneurysm	Lt ear	Pulsating ear, hard front		Ligation of veins in front of ear	Improved, but bruit per- sisted		Compression of both carotids stopped bruit, but not when one side was com- pressed
1935, Dunham	14, M	Multiple ar- teriovenous aneurysms	Back of head and neck, and intra- cranial	Pain in left eye, blowing sounds, throbs, pul- sations behind mastoids and down back to clavicle		Not treated			Multiple aneurysms between exter- nal jugular vein and internal carotid artery
1938, Reid and McGowan	19, M	Arteriovenous aneurysm	Rt side of neck and face	Swelling, and swelling in ear		Ligation of external carotid artery, ligation of occipital artery, division and twisting of external jugular vein	Cured		
1938, Reid and McGowan	19, M	Multiple ar- teriovenous aneurysms	Neck, Rt front, and face area	Slight bulges of ante- rior pulsating masses, marked thrill, hard front		Excision of external an- eurysm of arm and foot External excision of ear and aneurysm of neck Ligation of right external carotid artery	Arm and foot cured; neck markedly improved		14 finite aneurysms re- sulting with nar- rowed arteriovenous communications then cured
1938, Lewand	6, M	Multiple ar- teriovenous fistulas	Rt, side of neck	Pulsating lumps in neck, capillary bruit		Ligation of two small fistulas between common carotid and internal jugular veins; excision of internal jugular veins	Cured		

1938, Flinn?	19, F	Multiple ar- teriovenous fistulas	Left side of neck	Roaring, voice dilated veins in neck, continu- ous thrill and bruit	Ligation of multiple ar- teriovenous connections between veins and com- mon and internal carot- id, excision of internal jugular vein	Cured	Horsemans vessel
1938, Horton and Hempstead	53, F	Arteriovenous fistulas	Posterior to left ear	Noise in ear, continuous bruit and thrill	Ligation of arteriovenous communications between posterior right temporal artery and vein, and au- ricular artery and vein, ligation of temporal ar- tery and vein	Cured	No pulsations visible, compression of right posterior auricular artery caused bruit to cease
1938, Horton and Hempstead	43, F	Arteriovenous arteriove- nous fistula	Left external auditory canal, tongue, left arm and hand	Pain in ear, multiple angu- sours on tongue, throbb- ing noise in ear, in- creased vasculature of head and neck, and left arm and hand	Not treated		Various bluish showed increased oxygen
1940, Ward and Horton	19, F	Hemangioma and arterio- venous fistulas	Right side of neck, face scalp and ear	Enlarged vessels, multiple continuous thrills and bruits, large birthmark	Ligation of right external carotid and vessels in mastoid region	Improved	.
1940, Ward and Horton	21, M	Arteriovenous fistula	Left mastoid	Enlarged veins, continu- ous thrill and bruit	Ligation of right occipital artery, coagulation of dilated veins	Improved	Bruit ceased when ad- jacent vessels were compressed
1940, Ward and Horton	4, M	Arteriovenous fistula	Right lower neck	Continuous bruit and thrill above right clavicle	Not treated		Found incidentally, bruit disappeared on pressure over right common carotid
1940, Ward and Horton	7, M	Arteriovenous fistula	Right lower neck	Pulsation, continuous bruit and thrill above right clavicle	Not treated		Found incidentally, bruit disappeared on pressure over right common carotid

2 A case of arteriovenous aneurysm involving the internal maxillary artery and veins of the pterygoid plexus is presented in which the lesion was visualized by thorotrast carotid arteriography.

The fistula was temporarily obliterated by ligation and transection of the external jugular vein, the external carotid artery and all its branches proximal to the fistula and by packing the internal maxillary artery with muscle. The size of the heart diminished after the fistula was obliterated. The preoperative blood pressure was 115/60, two hours after operation it was 134/88 and one month after operation it was 124/80. Two and one half months after operation a faint bruit recurred due to collateral blood supply from the right external carotid.

The left half of the mandible was larger than the right as disclosed by accurate measurements of roentgenograms.

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CAROTID BODY TUMOR IN ASSOCIATION WITH CAROTID SINUS SYNDROME

REPORT OF TWO CASES

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OUR observation of a case of carotid body tumor in association with carotid sinus syndrome stimulated an interest as to the frequency of occurrence of such cases.

In a report of two cases of carotid body tumor in 1945, Dickinson and Traver¹ stated that about 275 cases have now been reported in the literature. Rankin and Wilfrock²³ in 1930 adding twelve cases of their own, brought the number of cases reported to an accurate total of 196. In a complete review of the English literature we were able to find reports^{2, 4, 11, 16} of four patients in each of whom there was a tumor in the neck, pressure upon which caused fainting. Each tumor was found in the region of the bifurcation of the common carotid artery, it operated and removed. Reports^{2, 4, 7, 10, 13, 14, 17} were found of ten patients who seemed to have had carotid body tumors in association with carotid sinus syndrome but the reports were open to some question due to the absence of actual syncope or omissions in the articles of discussions of operative removal. The review of the foreign literature although not complete disclosed two case reports^{1, 12} which were unquestionably cases of carotid body tumor in association with carotid sinus syndrome.

CASE REPORTS

CASE 1 (No. 1-3362).—H. M., a white male of 15 years was admitted to the Vanderbilt University Hospital April 12, 1944 complaining of fainting and a lump in the neck. For two years prior to admission he had had periods of loss of consciousness, the duration of which was from a few seconds to several minutes. He noted that the rapid turning of the head precipitated the attacks and that the wearing of tight collars increased the frequency with which they occurred. Preceding the loss of consciousness there was pain in the eyes, blurring of vision and lizziness. When the patient was lying down the latter three symptoms occurred sometimes but there was never loss of consciousness. He was sitting or standing. One year before admission he discovered a lump in the left side of the neck and he noted that pressure upon the mass caused the attacks. There had been a slow, slight increase in the size of the mass over a period of one year.

Past History.—In the Vanderbilt University Out Patient Department June 8, 1943, the patient was found to have a positive blood Wassermann reaction. He had been treated with bismuth and neocrylenamine.

Physical Examination.—Just posterior and inferior to the angle of the left mandible there was a firm nontender mass about 3 cm. in diameter which was movable laterally but not vertically. Following pressure upon the mass the patient became pale and lost consciousness, the blood pressure fell and the pulse decreased in rate (Table I).

Upon release of pressure the patient rapidly regained consciousness with no apparent ill effect.

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TABLE I THE EFFECTS UPON BLOOD PRESSURE AND PULSE RATE OF PRESSURE UPON THE CAROTID BODY TUMOR (CASE 1)

	BLOOD PRESSURE	PULSE
Normal	120/70	86
Orbital pressure	120/70	80
Right carotid sinus pressure	120/70	80
Left carotid sinus pressure		
During attack	Could not be obtained	52
30 Seconds after release of pressure	90/40	68
45 Seconds after release of pressure	100/40	80
60 Seconds after release of pressure	120/70	80

Operation—Under intratracheal nitrous oxide oxygen ether anesthesia through an incision along the anterior border of the sternocleidomastoid muscle the carotid sheath was exposed. A hard nodular mass concealed the bifurcation of the common carotid artery. The vagus nerve appeared at first to be incorporated in the tumor but was successfully freed from it. The tumor was incised in order to attempt to free it from the internal and external carotid arteries but no line of cleavage could be found. Accordingly, the common carotid artery and the internal jugular vein were ligated and divided below the tumor. The external and internal carotid arteries and the internal jugular vein were ligated and divided above the tumor. The mass was removed in one block along with a portion of the cervical sympathetic chain and the superior laryngeal nerve, to both of which the tumor was adherent. The wound was closed with silk.

During induction of anesthesia pressure upon the tumor caused temporary cessation of the heartbeat. After anesthesia had been induced further pressure upon the tumor nor upon the vagus nerve caused any change in the heart rate. During the first hour of the operation the blood pressure ranged around 150/70, then gradually rose to 180/70, with a rise in pulse rate from 100 to 100. After the administration of the anesthetic had been discontinued, the blood pressure fell gradually to 150/70.

Postoperative Course—The postoperative course was uneventful except for the presence of hoarseness and, on the left side, slight ptosis of the eyelid, miosis and slight decrease in sweating, but no demonstrable enophthalmos. On the first day after operation the left retinal vessels were decreased in size but contained blood. There was no muscular weakness at any time. Eight days after operation, laryngoscopic examination showed complete paralysis of the left vocal cord.

Pathologic Changes—Gross—The photograph (Fig. 1) shows the gross specimen. The tumor was 3 cm in diameter irregular nodular, and hard. The cut surface was white. The tumor had grown into the outer portion of the wall of the carotid vessels.

Micoscopic (Figs. 2 and 3)—The tumor cells grew in nests and strands, surrounding small blood vessels in many areas. Some of the cells had eosinophilic cytoplasm with indistinct cell borders and nuclei which were round or oval and densely basophilic. Other tumor cells were distinctly different, their cytoplasm being less eosinophilic and their nuclei less basophilic. The stroma was dense connective tissue. The tumor had invaded the adventitia of the common carotid artery. The appearance was that of a carotid body tumor or adenoma. Although this neoplasm showed a characteristic of malignancy in that it had invaded adjacent structures such tumors usually do not metastasize and are not considered truly malignant.

Follow up—There were no attacks subsequent to operation. On Dec. 30, 1946, two and one half years after operation a nontender mass 1 by 2 by 2 cm in size was felt in the region of the bifurcation of the right common carotid artery. Pressure upon this mass caused no symptoms. There was no recurrence of the tumor which had been removed from the left side of the neck. The patient has been advised to enter the hospital for removal of the tumor in the right side of the neck which is thought to be a carotid body tumor.

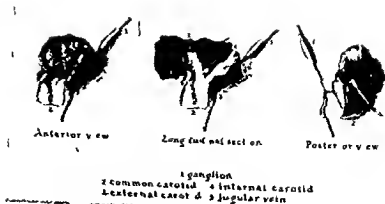


Fig 1 (Case 1)—Photograph of drawing of gross specimen



Fig 2



Fig 3

Fig 2 (Case 1)—The lumen of the common carotid artery is on the left; the wall of the vessel has been invaded by the neoplasm ($\times 70$).

Fig 3 (Case 1)—Tumor cells of the two types normally present in the carotid body ($\times 17$).

CASE 2 (No 154780).—L. M. B., a white woman of 23 years was admitted to the Vanderbilt University Hospital, Oct. 1, 1946, complaining of a lump in the neck. Eight years before admission, when her head was suddenly drawn backward, she fainted, she had a similar attack several weeks later. Subsequently, on many occasions, estimated by the patient to be between 50 and 100, she fainted after arising quickly or raising the head suddenly. The periods of unconsciousness varied from a few seconds to two minutes. The attacks had become less severe during the three years before admission, that is, syncope had been replaced in most of the attacks by a feeling of faintness not followed by actual fainting. Three years before admission she noted a definite mass in the left side of the neck but she had been conscious of a feeling of fullness in that region for several years previously. She had had buzzing in the left ear and frontoparietal headaches. One month before admission she noted a decrease in size of the left side of the tongue. When she first presented herself for treatment six weeks before admission she refused to permit examination of the tumor, stating that pressure would cause her to faint.

Physical Examination.—Posterior and inferior to the angle of the left mandible there was a hard, nodular, slightly tender mass, 5 cm. in diameter, which was very slightly movable laterally but not movable vertically. Pressure upon the mass caused neither subjective manifestations nor change in the pulse rate. There was atrophy of the muscles of the left side of the tongue. There was slightly decreased sensitivity to light touch over the entire left side of the face, slight drooping of the left eyelid and left corner of the mouth, and slight difficulty in swallowing. There were no other motor or sensory deviations from the normal.

Operation.—Under intratracheal nitrous oxide oxygen ether anesthesia, a transverse incision was made below the ramus of the left mandible and extended upward and posteriorly. The tumor, which was hard and surrounded by dense fibrous tissue, was found at the bifurcation of the common carotid artery. The mass completely encircled the carotid vessels and no line of cleavage between tumor and artery could be established. The common carotid artery was ligated and divided. The hypoglossal nerve, which emerged from the inferior portion of the tumor, was divided. The glossopharyngeal nerve and the superior and recurrent laryngeal nerves were not identified. The tumor was dissected free upward as far as possible but identification of the external and internal carotid arteries was impossible. Clamps were placed across the upper tip of the tumor and the mass was removed. The tissue included in the clamps was sutured and the wound was closed with silk.

Throughout the procedure the blood pressure ranged around 110/60 and the pulse from 90 to 100.

Postoperative Course.—On the first day after operation the patient had difficulty in swallowing but no weakness of the extremities. On the second postoperative day she developed right hemiplegia. An electroencephalogram was done without overventilation. The pattern contained a number of slow waves with a frequency as slow as three or four per second. They were more numerous on the left side in the temporal lead than elsewhere, although the parietal lead also had many such slow waves. Both frontal leads had some slow waves but there was marked similarity in them. The occipital leads also were similar and had fewest slow waves. Some of the slowness in the tracing could have been due to sedation but there was no difference in the two sides. There was return of some motor power the next day and the clinical manifestations of hemiplegia had cleared up completely forty-eight hours after its onset. Laryngoscopic examination two weeks after operation showed complete paralysis of the left vocal cord.

Pathologic Changes, Gross.—The tumor was 4 by 3 by 2 cm. in size, very firm and grayish white on the cut surface. The mass completely encircled the distal 2 cm. of the common carotid artery and the proximal centimeter of the external and internal carotid arteries. The lumina of the common and external carotid arteries were patent but that of the internal carotid was occluded.

Microscopic (Figs. 4 to 7).—The cells grew mainly in nests, exhibited the same perivascular arrangement as those in Case 1, and were the same two types of cells. The stroma was



Fig 4 (Case 2) —The lumen of the common carotid artery is on the left; there has been invasion further centrally in the vessel wall than in Fig 2 (X²⁰⁰)



Fig 5 (Case 2) —Two types of tumor cells growing in nests surrounding small blood vessels (X³²⁰)

ten a fibrous tissue. The tumor cells extended into the media of the common carotid artery. The lumen of the internal carotid artery was occluded by a thrombus. Numerous blood vessels and nerves were present. The microscopic findings are characteristic of carotid body tumor or adenoma. The tumor had invaded adjacent structures but it was not considered to be malignant.

Follow up—Jan. 31, 1947, nearly four months after operation the patient stated that there had been no recurrence of tumor, syncope, or headache, but that she still had buzzing in the left ear. Examination showed slight induration and tenderness in the region of the scar.



Fig 6 (Case 3) The lumen of the external carotid artery is patent (X 60).

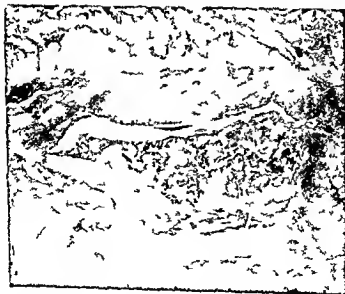


Fig 7 (Case 3)—The lumen of the internal carotid artery is blocked by a thrombus (X 60).

Comment—The carotid sinus syndrome is usually the result of a reflex initiated by the stimulation of a hypersensitive carotid sinus. Weiss and Baker¹ described three types of this syndrome: (1) The vagal type in which there is slowing of the pulse rate or asystole with or without fall in the blood pressure, (2) the depressor type in which there is fall in the blood pressure without slowing of the pulse rate, and (3) the cerebral type in which there is diminution of the cerebral circulation without slowing of the pulse rate or fall in the blood pressure. The mechanism of syncope in the third type is not clear, it might conceivably be due to local vasoconstriction of the common or the internal carotid artery.

Two possible explanations of the spontaneous disappearance of the carotid sinus syndrome are suggested. First, the facts that the lumen of the left internal carotid artery of this patient was not patent and the absence of preoperative muscular weakness on the right side indicate that collateral circulation had been developed. The occurrence of hemiplegia on the right side following removal of the tumor from the left side is evidence that the collateral circulation had been on the left. At the time the collateral circulation became adequate to render the central area independent of blood from the internal carotid artery, the carotid sinus syndrome disappeared. In order to accept this hypothesis one must grant the premise that the patient's carotid sinus syndrome was of the cerebral type and that that type is due to local vasoconstriction of the internal carotid artery.

The carotid sinus nerve may be connected with the trunk, inferior laryngeal and pharyngeal branches of the vagus nerve, the superior cervical sympathetic ganglion, and the trunk of the glossopharyngeal nerve, the latter being its principal and most constant afferent connection.² A second and more likely reason for the disappearance of the carotid sinus syndrome in this patient is that the tumor destroyed the afferent nerve connection or connections from the carotid sinus, thus breaking the reflex arc necessary to produce the carotid sinus syndrome.

SUMMARY

A case of carotid body tumor in association with carotid sinus syndrome of the vagal type is presented. Cure was effected by extirpation of the tumor with segments of the common, external, and internal carotid arteries.

A second patient with carotid body tumor is described who gave a typical history of carotid sinus syndrome which disappeared spontaneously. Two possible explanations of the spontaneous disappearance of the syndrome are given.

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EARLY CLINICAL RESULTS OF TRANSABDOMINAL CELIAC AND SUPERIOR MESENTERIC GANGLIONECTOMY, VAGOTOMY OR TRANSTHORACIC SPANCHNICECTOMY IN PATIENTS WITH CHRONIC ABDOMINAL VISCERAL PAIN

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THE abdominal viscera receive motor innervation from the sympathetic and parasympathetic divisions of the autonomic nervous system. The splanchnic and the parasympathetic nerves also carry visceral sensory pathways. Somatic pathways overlap visceral pathways only at attachments to the diaphragm or to the peritoneum of the posterior abdominal wall or pelvis.

Effects of interrupting visceral motor innervation by dividing splanchnic or vagus nerves or of interrupting sacral autonomic pathways have been extensively described in the literature and will not be reviewed. Effects of interrupting visceral sensory pathways have been less extensively studied. Occasionally relief from abdominal pain after splanchnic block or splanchnicectomy has been described. Isolated reports have indicated that appendicitis, cholecystitis or peptic ulcer developing after bilateral splanchnicectomy for hypertension have caused little or no pain. The concept that abdominal visceral pain is mediated by sensory pathways traveling in the splanchnic nerves is generally accepted and has been confirmed by Ray and Neill.¹

The miscellaneous studies and operations to be reported were carried out to reinvestigate pathways for visceral pain and to determine possible utility of operations designed to interrupt these pathways. They deal with five problems related to abdominal visceral pain. The first is the possibility that pathways transmitting pain may travel through the vagus nerves. The second concerns the role that vagotomy or splanchnicectomy might play in relieving pain or vomiting occurring during gastric crises of tabes dorsalis. The third is the effect of extensively excising the celiac and superior mesenteric ganglia in patients with so-called biliary dyskinesia. The fourth is the possibility that celiac and superior mesenteric ganglionectomy combined with subdiaphragmatic vagotomy might aid patients with severe unexplained abdominal pain of so-called functional bowel distress. The fifth problem deals with celiac and superior mesenteric ganglionectomy for pain from chronic pancreatitis. This report of these studies is of a preliminary nature since only a few patients have been observed a short period of time.

STIMULATION OF THE VAGUS NERVES

The possibility that visceral pain might be controlled by interruption of the vagus nerves has been revived since Dragstedt and Schafer² reintroduced

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vagotomy as a treatment for peptic ulcer. With others^{3,4} they demonstrated that intractable pain from ulcer when present before operation is relieved by the time patients recover from anesthesia and before ulcers could heal. This phenomenon has not been adequately explained by changes of gastric acidity or motility.⁶ Moore and associates⁴ have demonstrated that excessive distention of balloons in the intestinal tract produces pain after vagotomy. Our patients with vagotomy for peptic ulcer have experienced pain from strangulation of a Meckel's diverticulum or from cholecystitis.⁵ Nevertheless the prompt relief from pain of ulcer after vagotomy simulates sensory denervation. The following tests therefore were undertaken to determine whether pain pathways might be present in the lower thoracic or abdominal distribution of the vagus nerves.

In two patients each main trunk of the vagus at the level of the hiatus of the diaphragm was stimulated mechanically by pinching during transabdominal operation for peptic ulcer under spinal anesthesia extending up to the fourth thoracic dermatome. Neither patient experienced pain. Stimulation of each main trunk three inches above the diaphragm faradically and then by pinching produced pain referred to the neck in two other patients during transthoracic vagotomy under spinal anesthesia extending to the third and fourth thoracic dermatomes. The nerves were then divided. Faradic stimulation of the distal end had no effect but similar stimulation of the proximal end produced pain referred to the neck. Physiologic section proximal to the point of electrical stimulus stopped this pain. As spinal anesthesia diminished in one patient stimulation of the proximal end of a divided left major splanchnic nerve produced a sensation of intense abdominal pain.

An intact left vagus nerve was exposed in the neck of another patient using local anesthesia and stimulated electrically without blocking splanchnic afferents by spinal anesthesia. This produced pain referred to the neck and also a sensation described as sour stomach or heartburn. Because of negative results in patients under spinal anesthesia it is assumed that this sensation was produced by motor stimulation of the stomach and that the resulting discomfort was probably mediated by splanchnic sensory pathways.

TRANSTHORACIC VAGOTOMY OR BILATERAL SPANCHNICECTOMY FOR GASTRIC CRISES OF TABES DORSALIS

Although the mechanism of pain during gastric crises of tabes dorsalis is not well established patients have been treated variously by dorsal rhizotomy, chordotomy, vagotomy and splanchnicectomy or splanchnic block. As early as 1911 Funes divided both vagi in two patients without relief. It is of interest that both subsequently required gastroenterostomy because of 'ill effects of paralysis of the stomach.' Pearl⁷ reported relief in one patient after interrupting sympathetic and vagal pathways traveling through the celiac ganglia by excision of both ganglia and removal of the adjacent periaortic sympathetic plexus. Our observations deal with transthoracic vagotomy in two patients and with bilateral splanchnicectomy in another.

Transthoracic vagotomy was performed in two patients with *tabes dorsalis* complicated by repeated incoordinating gastric crises. It was hoped that reduction of peristalsis and volume of gastric secretions following vagotomy would reduce severity of attacks. The first patient, a 35 year-old man had had attacks of pain at approximately monthly intervals for six years. After vagotomy, crises recurred with frequency and severity equal to that before operation. The second patient a man of 25 years, had had attacks of pain about every other month for five months. After vagotomy, obstruction at the outlet of the stomach developed with gastric retention, and a secondary gastroenterostomy was necessary. Crises recurred and became more frequent and severe. Four months later a bilateral dorsal chordotomy was performed. Alcoholism and drug addiction led to confinement in a psychiatric hospital.

The third patient a 29 year old woman with gastric crises, was treated by bilateral thoracolumbar sympathectomy and splanchnicectomy using the posterior Smithwick approach. She had had epigastric and right abdominal pain and vomiting almost continuously for ten months most of which time she was in the hospital. Splanchnic block by procaine relieved pain during an attack. After right sympathectomy and splanchnicectomy, relief from abdominal pain was almost complete but nausea and vomiting continued. Several months later left upper abdominal pain developed to a degree equal to that originally present on the right. One year later a left lumbodorsal sympathectomy and splanchnicectomy were performed. Abdominal pain was then less severe, but vomiting continued. Intractable pain then developed in the right side of the chest and neck and this together with lightning pains in the arms and legs led to chordotomy between the second and third thoracic segments. During the next two and one-half years the patient had less vomiting and only infrequent episodes of mild pain.

RIGHT CELIAC AND SUPERIOR MESENTERIC GANGLIONECTOMY FOR "BILIARY DYSKINESIA"

The cause of attacks of right upper quadrant pain recurring after cholecystectomy is not known. Smithwick and Chapman⁹ have employed unilateral or in some cases bilateral splanchnic denervation in about a dozen patients with attacks of pain following surgery of the biliary tract and studied them before and after surgery by balloon distention tests. A little over one-half of the patients have been relieved for considerable periods of time. Womack¹⁰ postulated that pain might be associated with neuromas which he has observed about the bile duct after cholecystectomy. Exploratory laparotomy is often indicated in biliary dyskinesia to rule out stones in the common duct pancreatitis or abnormal narrowing of the opening through the ampulla of Vater. Since pain frequently recurs after operation the possibility that relief might be obtained by interrupting sensory pathways at the time of exploration and through the abdominal incision has been investigated. A modification of the operation used for hypertension by Crile¹¹ which removes the celiac ganglia and interrupts the sympathetic complex¹² about the aorta has been adopted.

The operation is illustrated in Fig 1. After exploration of the abdomen and the common duct the gastrohepatic ligament is incised medial to the portal vein. The stomach and the liver are then retracted to expose the aorta near the celiac axis. Fibers of the periaortic sympathetic plexus are then located and traced to the right celiac ganglion. Occasionally the splanchnic nerve itself can be identified as it comes through the diaphragm and traced. The right celiac ganglion is then mobilized by traction and freed by division of its smaller branches. Traction on the ganglion and retraction of the celiac and superior

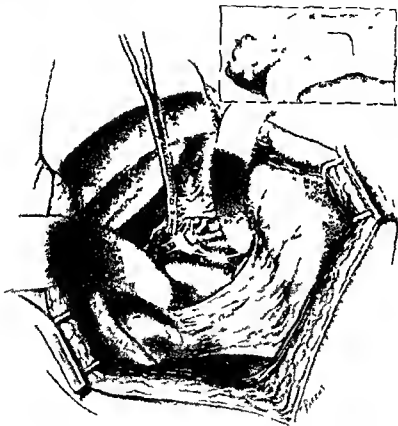


Fig 1. The celiac and superior mesenteric ganglia are exposed and retracted through a transverse or oblique incision in the abdominal wall and a longitudinal incision in the gastrohepatic ligament.

mesenteric artery permit tracing of the larger communications to mobilize and excise varying portions of the left celiac and the superior mesenteric ganglia. The superior mesenteric ganglion often can be pulled out from under the superior mesenteric artery almost entirely and everted. The left celiac ganglion is exposed directly by dissection to the left of the celiac artery if desired.

Four patients with recurrent episodes of right upper quadrant pain of the so-called 'biliary dyskinesia' type have been treated. Each had had

cholecystectomy followed by recurrence of episodes of right upper quadrant colicky pain resembling those preceding removal of the gall bladder. Although jaundice had not occurred, symptoms were severe and exploration of the common duct was considered advisable. In each patient exploration of the abdomen revealed no adequate explanation for pain. The common duct was explored and the ampulla of Vater was moderately dilated. T tubes were placed in the common duct. In two patients these tubes were injected with saline solution under pressure ten days after operation*. One patient experienced no discomfort with pressures as high as 230 mm water, and the other experienced only moderate discomfort in the left flank.

The clinical effects of operation as determined by a short period of observation have been variable. Good results were obtained in three of the four patients. The first was a 38 year old woman who had had frequent attacks of "gall bladder colic," occasionally with jaundice, for two years and then cholecystectomy. She was told that the gall bladder contained numerous small stones. Fifteen days after cholecystectomy, attacks of pain without jaundice recurred. During the next year the longest interval between attacks was three weeks. Exploration of the common duct and right celiac and superior mesenteric ganglionectomy were then performed and during a period of observation of six months there have been no further attacks.

The second patient was 28 years of age at the time of ganglionectomy. Four years and four months earlier the gall bladder had been removed because of six months of recurring episodes of right upper quadrant pain associated with jaundice, chills, and fever. She was told that the gall bladder did not contain stones. After this operation she was well for four years and then severe episodes of right upper quadrant pain recurred. Each episode lasted from ten days to two weeks and was associated with nausea but not with jaundice. After four months of difficulty exploration and right celiac and mesenteric ganglionectomy was performed. Relief from pain followed and has continued eleven months. Incidentally this patient had dysmenorrhea before operation and now voluntarily states that menstruation is painless. We offer no explanation of this statement.

The third patient was 53 years of age at the time of removal of the right celiac and the mesenteric ganglia. She had had frequent attacks of right upper quadrant pain for twelve years. Jaundice and fever developed and the gall bladder was removed one year before ganglionectomy. She was told that there were no gall stones. Six weeks later pain recurred with episodes so frequent that the patient described "constant attacks." During twenty-one months that have elapsed since ganglionectomy she has been comfortable and regained lost weight. There have been two minor episodes of pain described as "indigestion" which she does not believe resemble the former pain.

The fourth patient has had little benefit. She was 32 years of age and had had numerous attacks of right upper quadrant pain without jaundice, chills or fever during four years preceding ganglionectomy. A gall bladder

*G. B. Hodge and A. L. Measer are reporting these and other studies of the neurophysiology of the gall bladder.

containing stones had been removed after the first year of difficulty. Pain recurred within two weeks and persisted. Exploration and right celiac and mesenteric ganglionectomy were performed. Soon afterward attacks were less frequent and painful but nine months after operation they were again frequent and severe. This patient suffers from an anxiety neurosis and is now again in bed much of the time with the sick spells.

An additional patient was treated by dividing only the main trunk of the right splanchnic nerve beneath the diaphragm. He had had intermittent pain for eighteen years. Cholecystectomy had been performed fifteen years before this operation and drainage of the common duct twelve years later. Severe attacks of pain continued. No explanation of the attacks was found during exploration of the common duct. Exposure was difficult due to obesity and faulty spinal anesthetic and consequently the right main trunk of the splanchnic nerve was divided without removing the ganglia. Attacks of pain similar to those before operation occurred two months later and have continued.

SUBDIAPHRAGMATIC VAGOTOMY AND CELIAC GANGLIONECTOMY FOR SEVERE UNEXPLAINED ABDOMINAL PAIN

Two patients with severe unexplained abdominal pain were treated by both celiac ganglionectomy and subdiaphragmatic vagotomy. The first patient was 34 years of age and had gradually developed dull gnawing epigastric distress often associated with nausea and vomiting. This more or less continuous complaint led to admission to five different hospitals and a diagnosis in each of functional bowel distress. On admission no definite abnormality could be discovered by detailed clinical and laboratory examination. Fluoroscopy revealed an increase in the peristaltic activity of the stomach and also occasionally reverse peristalsis of the duodenum. Sounds of accentuated intestinal movement were evident by auscultation at all times. Neuropsychiatric consultation confirmed the impression that symptoms were related in part to emotional problems. The patient had occasionally received morphine for pain. Nevertheless because of the seriousness of the condition exploratory laparotomy was considered advisable.

Operation was carried out under spinal anesthetic through a right transverse incision. Exploration of the entire abdomen revealed no pathology. The right celiac and a major portion of the superior mesenteric ganglia were removed. This produced no visible change of peristalsis. The vagus nerves and their branches were exposed at the hiatus of the diaphragm and excised. Following this peristalsis of the stomach ceased and the organ assumed a globular shape but did not dilate. Active peristalsis was evident in the duodenum and in the small intestine and colon.

Since operation epigastric pain and nausea have not recurred during a period of observation of seven months. This patient was readmitted however, twenty days after operation because of difficulty in swallowing as a result of food lodging in the lower esophagus. Barium swallow revealed no evidence of obstruction. These symptoms subsided after several days and have not recurred.

The patient was again admitted one month later because of emotional instability diagnosed as "simple adult maladjustment." She had been demanding morphine. After two weeks on the psychiatric service she returned home and has since returned to work, without medication, relieved of all former complaints. It is of interest that exaggerated peristaltic sounds are still audible and that transit time through the small intestine is rapid as judged by roentgenograms taken after ingestion of barium. Also, acidity of fasting gastric secretions has not been reduced and insulin hypoglycemia effected an increase of free acid to 80 clinical units.

The second patient with severe unexplained abdominal pain was 30 years of age at the time of vagotomy and ganglionectomy. Epigastric pain had occurred in progressively more frequent and severe attacks during three years and had been continuous for six months. Nausea or vomiting had not occurred. Sounds of intestinal movement were exaggerated. The fluoroscopist reported spasm of the second portion of the duodenum. Otherwise detailed examination revealed no definite abnormality. Exploration was considered advisable. At operation there was no evidence of disease and right celiac and mesenteric ganglionectomy and vagotomy was performed. Relief from pain followed and has persisted six months. There was marked reduction of free acid in the secretions of the fasting stomach. Also there was no elevation of free acid after insulin hypoglycemia or caffeine test meal. Fluoroscopic examination revealed sluggish gastric peristalsis with retention of 95 per cent of the barium after six hours. This patient has returned to heavy manual labor and is well satisfied except for the occasional occurrence of malodorous regurgitation of gas and a sensation of fullness of the stomach after eating large meals.

CELIAC GANGLIONECTOMY FOR CHRONIC PANCREATITIS

Whipple¹² has recently reviewed the surgical treatment of pancreatic fibrosis associated with calcareous deposits and emphasized the seriousness of chronic intractable abdominal pain. This disease is ordinarily treated by subtotal or total pancreatectomy. There is a possibility that pain may be relieved by division of the splanchnic nerves. Smithwick¹³ described relief from pain in one patient after right thoracolumbar splanchnicectomy. It is of interest that Marion,¹⁴ Ryces¹⁵ and others have described relief from pain of acute pancreatitis by splanchnic block using novocain. Our observations are limited to one patient. He was 33 years of age at the time of operation and for four years had had recurrent episodes of severe pain referred to the back and the epigastric region. During this time he had received hypodermic injections and had frequently taken alcohol. The last attack had continued seven weeks. He was formerly obese and had lost 128 pounds. At the time of operation he weighed 139 pounds. X-ray examination revealed patchy areas of calcification throughout the pancreas. The pancreas observed during operation was enormously enlarged and veins in the transverse mesocolon and about the pancreas were dilated and tortuous. There were also numerous adhesions. Pancreatectomy was not considered feasible. Removal of both celiac ganglia and of the superior mesenteric ganglion was performed.

Following operation pain was relieved for five months. During the next six months however, four episodes of severe back pain occurred, each requiring hospitalization. The patient has arthritis of the thoracic and lumbar spine, but during the last attack pain was also referred to the epigastrium.

DISCUSSION

The miscellaneous studies and the operations described in this preliminary report were undertaken to reinvestigate pathways for abdominal visceral pain and to determine whether operations designed to interrupt these pathways might have clinical value.

Evidence obtained by stimulation of the vagus nerves supports the concept that abdominal visceral pain is transmitted by sensory afferents through the splanchnic nerves and not through the vagus nerves.

Transthoracic vagotomy in two patients suffering with gastric crises of tabes dorsalis has not relieved pain, has led to gastric retention and therefore, seems contraindicated in this condition. Bilateral splanchnicectomy gave some relief from pain of gastric crises in one patient but recurrence of pain elsewhere subsequently led to chordotomy. It, therefore, seems probable that although splanchnic block by novocain may give temporary relief during attacks splanchnicectomy may be less advisable than chordotomy.

Right celiac and partial left celiac and superior mesenteric ganglionectomy have been employed during exploratory laparotomy in four patients suffering from so-called biliary dyskinesia. Three patients have been relieved of pain. This operation is not associated with serious disturbances of gastrointestinal function and may be of value when exploration has been performed without finding a stone in the common duct or other cause for pain.

Celiac ganglionectomy and subdiaphragmatic vagotomy were both performed in two patients with severe unexplained abdominal pain the cause of which was not found at operation. Although both patients had relief from pain, symptoms of gastric retention occurred. It seems probable, therefore, that ganglionectomy without vagotomy might be a better procedure. Ganglionectomy has partially relieved pain from chronic or recurring pancreatitis in one patient after laparotomy had demonstrated contraindications to pancreatectomy.

It is recognized that pain is a subjective observation and that controls have not been possible to determine whether psychotherapeutic suggestion has played a role in the relief of pain described. It is also recognized that observations have been limited to a few patients observed only a short period of time. Nevertheless since patients occasionally present problems of chronic abdominal pain sufficiently serious to warrant exploratory laparotomy and since operation does not always reveal the cause of pain, it is possible that subtotal to total excision of the celiac ganglia and of the superior mesenteric ganglion might be utilized as a supplement to exploration for relief from pain in these individuals. It is recommended that this operation be employed only after careful medical and psychiatric investigation and management have been undertaken.

The patient was again admitted one month later because of emotional instability diagnosed as "simple adult maladjustment." She had been demanding morphine. After two weeks on the psychiatric service she returned home and has since returned to work, without medication, relieved of all former complaints. It is of interest that exaggerated peristaltic sounds are still audible and that transit time through the small intestine is rapid as judged by roentgenograms taken after ingestion of barium. Also, acidity of fasting gastric secretions has not been reduced and insulin hypoglycemia effected an increase of free acid to 80 clinical units.

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VAGOTOMY FOR PEPTIC ULCER

EXPERIMENTAL AND CLINICAL STUDIES

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THE operation of vagotomy for peptic ulcer has been widely used since its revival by Dragstedt and Owens in 1913. The modern procedure differs from most of its predecessors in that it is undoubtedly more complete and is performed only near the level of the diaphragm. The nerves may be sectioned just above the diaphragm (transthoracic approach) or just below it (transabdominal approach). Other workers who have contributed to the recent study of this procedure include Weinstein, Colp, Hollander and Jemmett (1944), Moore, Chapman, Schulz and Jones (1946), Ruffin, Grimson and Smith (1946), Bradley, Small, Wilson and Walters (1947) and Miller and Davis (1947). It is felt that because of the current interest in the subject the report of any studies, either clinical or experimental, is appropriate at the present time.

EXPERIMENTAL STUDIES

In our laboratory five types of experiment were performed. Three of these showed no effect of the test procedure on the incidence of histamine provoked ulcer in the guinea pig. These negative experiments included transabdominal vagotomy, aqueous benadryl solution by mouth, benadryl in beeswax subcutaneously.

The histamine ulcers were produced by the standard method of Vaseo, Code, Walpole and Wangensteen (1941) using a histamine mineral oil beeswax mixture. None of the three methods previously listed prevented gastric ulceration in the guinea pigs. However, the possibility remains that if the doses of histamine were reduced to a level that would barely produce ulceration in the controls, vagotomy or benadryl might then have prevented or reduced the incidence of ulceration. We used full doses of histamine in beeswax and found no effect. Since starting these experiments Friesen, Baronofsky and Wangensteen (1946) reported that benadryl in beeswax fails to prevent histamine provoked ulcers in dogs.

The other two types of experiment which gave more positive results are as follows:

*The Effect of Vagotomy on the Development of Jejunal Ulcers in the Mann-Williamson Dog**—Beaver and Mann (1931) reported that three control Mann-Williamson dogs developed ulcer (100 per cent) whereas of three such dogs with supplementary transthoracic vagotomy only two developed ulcer (67 per

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and definite indications for exploratory laparotomy established. Ganglionectomy may be of value in patients suffering pain from visceral disease that cannot be treated surgically otherwise.

CONCLUSIONS

1 Preliminary observations suggest that excision of the right celiac ganglion and of part or all of the left celiac and the superior mesenteric ganglia will significantly interrupt pain pathways from the abdomen and can be used as an adjunct to exploratory laparotomy for relief from chronic pain arising from the abdominal viscera.

2 Vagotomy should not be employed for gastric crises of tabes dorsalis and probably should not be used at the time of ganglionectomy for visceral pain.

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fifteen hours of pyloric ligation, rats which have been previously starved regularly develop multiple hemorrhagic ulcerations of the gastric rumen. In some instances, ulcers of the fundus are also observed. To our knowledge, the effect of vagotomy on the development of such ulcers has not been previously reported.

Technique—Littermate albino rats of the Sprague Dawley strain weighing about 200 grams were starved for seventy two hours, but were allowed water ad libitum up to the time of pyloric ligation. During the entire experiment the animals were kept in cages with wide mesh wire bottoms to prevent eating of excreta.

The operative procedure was performed under intraperitoneal pentothal anesthesia supplemented by a small amount of ether by inhalation. With aseptic precautions the stomach was exposed through a short vertical epigastric incision and the pylorus was snugly ligated with a double ligature of silk in all animals. In the vagotomized half of the series the vagus nerves were ligated infra diaphragmatically where they lay in proximity to the esophagus. This was done by the method similar to that which one of us (H N H) learned in the laboratory of Dr C Heymans in Ghent for another purpose. Heymans' technique of ligating the nerves to the carotid sinus was to put the ligature under the carotid arteries and then to ligate everything else. In the present experiments, the ligature was put under the carefully freed esophagus and then all contiguous fibers except the esophagus were tied. In the control rats the esophagus was carefully freed from the surrounding nerves exactly as for vagotomy, except that nothing was tied. The abdominal wound was then resutured and the animals were returned to their cages. They were then either sacrificed with ether at the end of about twenty four hours or kept alive as long as possible (with almost daily injections of 10 to 15 cc of glucose saline solution) to determine the length of survival.

Twenty four hour results All of the seventeen rats in the control series had ulcers of the gastric rumen and seven of them had, in addition, ulcers of the fundus of the stomach. As seen in Table III, there were 316 small ulcers and 37 large ulcers (that is larger than 4 mm in their greatest diameter). There was an average of twenty two ulcers of the rumen in each rat. One animal had a perforated ulcer at the time of death thirty one hours after operation. His

TABLE III THE EFFECT OF VAGOTOMY ON ULCER DEVELOPMENT IN THE RAT'S GASTRIC RUMEN AFTER PYLORIC LIGATION (TWENTY FOUR HOUR RESULTS)

	17 CONTROL RATS	15 VAGOTOMIZED RATS
Small ulcers	316	0
Large ulcers (> 4 mm)	37	0
Perforations	1	0
Fundus ulcer present	7	0
Volume gastric fluid (cc av)	14	7
Free acid units (av)	17	7
Total acid units (av)	81	56

TABLE I THE EFFECT OF TRANSTHORACIC VAGOTOMY ON ULCER DEVELOPMENT IN THE MANN WILLIAMSON DOG*

NUMBER OF DOGS	NUMBER OF ULCERS	PER CENT
3 Control Mann Williamson	3	100
3 Vagotomized Mann Williamson	2	67

*Beaver M. G. and Mann F. C. Ann Surg 54 1116-1118 1931

cent) (see Table I) The importance of this experiment is so obvious that it was thought advisable to repeat it using a larger number of animals

The typical Mann Williamson operation described by these authors in 1923 involves a transection of the pylorus and of the jejunum. The duodenal stump is closed, the open end of distal jejunal loop anastomosed to the pyloric end of the stomach, and the open end of the proximal jejunal loop to the distal ileum. This technique provides a gastrojejunostomy with no chance for neutralization of the gastric juice by bile, pancreatic secretion, or other duodenal juice. Most of the dogs with such an operation develop a typical jejunal ulcer, usually about 1 cm. away from the suture line, and die from perforation, hemorrhage or malnutrition in from one to three months.

TABLE II THE EFFECT OF TRANSTHORACIC VAGOTOMY ON THE DEVELOPMENT OF JEJUNAL ULCERS IN MANN WILLIAMSON DOGS

NUMBER OF DOGS	AVERAGE (DAYS)	PER CENT
23 Mann Williamson		
13 controls		
11 developed ulcer survival 29 to 161 days	64	85
2 died with no ulcer survival 55 to 145 days	100	
9 With vagotomy		
1 developed ulcer survival 41 days		11
	118	
	318	
	169	

As seen in Table II in our series of thirteen control Mann Williamson operations eleven dogs died with ulcer (85 per cent) after 29 to 161 days (average interval 64 days) following the operation. Two dogs, dying 55 and 145 days after the operation, had no ulcer. In the series of nine dogs with the Mann Williamson operation plus a supplementary transthoracic vagotomy only one died with ulcer (11 per cent) forty-one days after operation. Six of these dogs died from 28 to 197 days (average interval, 118 days) following the Mann Williamson operation and presented no signs of ulcer. Two additional dogs with the combined procedure were still alive 206 and 430 days after the Mann Williamson operation, an average of 223 days. It should be pointed out that in the control series no animals were included unless they lived at least four weeks after the Mann Williamson operation.

The Prevention by Vagotomy of Pyloric Ligation Induced Ulcers of the Gastric Rumen of Rats—In 1945, Shay and associates reported that within

tentatively that the vagotomies performed with shunts or gastric resections have, on the whole, done better than when no complementary procedure was performed. The vagotomies with gastric resection have differed little from the postoperative course of a similar group of gastric resections alone (Grose and Johns). A careful follow up study has been made and is still in progress concerning the entire series. On the basis of this study a few preliminary observations can be made.

Of the total thirty six cases, twenty eight patients have been seen in the outpatient department within the past two months. A postoperative insulin test by the method of Hollander (1946) has been done on seventeen patients with fourteen nonreactive findings and three reactive tests. Of the three reactive cases two patients have been reoperated upon with positive findings of remaining or recurrent ulcer. One transthoracic patient had a reactive (positive) insulin test, but is doing as well symptomatically as any patient in the entire series.

The symptomatic results of the operation are

- (1) Marked relief of pain
- (2) Relative diarrhea
- (3) Delayed gastric emptying time

The relief of pain has been an almost constant finding and occurs quite promptly. The patients are, on the whole, very grateful for this relief and consider its benefits as greater than the disadvantages of some of the other maltoward symptomatic effects. The relative diarrhea has been noted in about four fifths of the cases. Since some patients were constipated before operation, it may manifest itself in these cases by a restoration of normal bowel habits, whereas in those patients who were normal in this regard before operation, a true and occasionally troublesome diarrhea develops. In general, this symptom improves as the time since operation grows greater.

Delayed gastric emptying time has been noted in many cases. Urecholine has been tried in three cases and has given some relief. Some patients have a symptomless gastric distention whereas others vomit frequently. Again, this symptom abates in the late postoperative period.

Four cases in the series of thirty six can already be classed as clinical failures. As previously stated, if the insulin test is an accurate index of the completeness of vagotomy in two of these patients the vagotomy was not complete and the failure cannot be blamed on the procedure. The four cases are reported here.

CASE 1—A man aged 31 years had continued pain despite a transthoracic vagotomy on Aug. 13, 1946. One insulin test showed a nonreactive state while the second was positive or equivocal. An active duodenal ulcer was found at the second operation and a gastric resection was done.

tologically, the ulcers were deep, some involved most of the layers of the stomach wall, and there was an associated extensive edema. On the other hand, in the fifteen vagotomized rats there were no ulcers of the rumen or fundus and there was no edema of the stomach wall demonstrable on microscopic examination.

The control animals had an average of 14 c.c. of fluid in the stomach while the vagotomized rats averaged 7 c.c. In the control series the gastric fluid was more acid than in the vagotomized animals (free acid 17 and 7 units respectively, total acid 81 and 56 units) *.

Results of survival experiments—Six rats with pyloric ligation survived an average of forty six hours, whereas seven rats with pyloric ligation plus supplementary infradiaphragmatic vagotomy survived an average of ninety seven hours.

Comment—Irrespective of whether the lesions produced by pyloric ligation are ulcers or deep hemorrhagic erosions, at least they are prevented by vagotomy during the twenty four hour time limit under discussion. Neither diminished acidity nor decrease in the volume of gastric contents is the only factor which will explain the beneficial effect of vagotomy. Certain control rats developed ulcers despite a lower acidity or a lower volume of gastric contents than was observed in certain vagotomized rats, none of which had ulcerations.

PRELIMINARY CLINICAL OBSERVATIONS†

Vagotomy of the modern complete type was done for peptic ulcer in the Johns Hopkins Hospital in only two instances before May 14, 1946. Both of these preliminary operations in 1945 were performed through the right side of the chest, and were accompanied by bilateral splanchnectomy. Both patients had a recurrence or a development of a new peptic ulcer.

On May 14, 1946 Shumacher did the first of the new series of vagotomies for peptic ulcer and up to Feb. 1, 1947 a total of thirty-six operations had been performed including the two done in 1945. As seen from Table IV the cases fall into several groups as far as the type of operation is concerned so that it is difficult to compare the results of the different procedures. It can be said very

TABLE IV. CLINICAL VAGOTOMIES—THIRTY-SIX CASES (SEVEN PRIVATE, TWENTY-NINE WARD CASES)

OPERATION	NUMBER OF CASES
Vagotomy alone	1
Transabdominal 1	
Trans thoracic 11	
Transabdominal vagotomy plus esophagotomy 6	9
Gastroenterostomy 2	
Pyloroplasty 2	
Vagotomy plus gastric resection	13
Transabdominal 11	
Previous trans thoracic vagotomy plus splanchnectomy (in 1945) 2	

*The gastric analyses were performed by Mr. Stuart R. Elliott, II.

†The authors acknowledge the cooperation of Dr. Thomas Johns, Dr. Moses Paulson, Dr. William L. Grose, and Dr. Eugene Gladstein.

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CASES 2 AND 3—Two patients with coincident splanchnicectomy both had secondary resections. In one instance a large gastric ulcer was found at the secondary operation. The insulin test was reactive in one case and was not done in the other.

CASE 4—J H, a 59 year old man, a clerk, had severe postprandial pain for two months. Roentgen examination revealed a penetrating ulcer of the lesser curvature of the stomach.

First Admission—At laparotomy on July 1, 1946, an anterior gastric ulcer midway up the lesser curvature was biopsied. Chronic inflammatory tissue was the only finding and there was no sign of malignancy. An abdominal vagotomy was done and the ends of the nerves were sutured to the diaphragm. The patient was discharged on July 18, 1946, with no symptoms, although roentgen examination showed definite gastric retention.

Interval—The patient developed diarrhea, a sense of fullness, and vomiting, but had absolutely none of the old ulcer pain and he gained nine pounds in weight. Roentgen examination showed a twenty four hour retention and gastroscopy showed a fifteen hour retention. An insulin test done on Sept 13, 1946 (with a hypoglycemia of 22), showed no free acid (negative nonreactive).

Second Admission—After three days of constant suction, a laparotomy was performed on Feb 6, 1947. The stomach was found to be small, the gastric ulcer was healed leaving only a small scar, and the pylorus easily admitted the tip of an index finger. A gastroenterostomy was performed.

Comment—This case is of especial interest since it shows that the gastric distention and delayed emptying time following vagotomy can occur independently of true cicatricial pyloric obstruction.

SUMMARY

1 In a series of thirteen control Mann-Williamson dogs, the incidence of jejunal ulcer was 85 per cent. In a series of nine Mann-Williamson dogs with transthoracic vagotomy, only one (11 per cent) developed jejunal ulcer.

2 Pyloric ligation induced ulcers of the gastric rumen of rats developing within twenty four hours were prevented by transabdominal vagotomy (control series 346 ulcers in 17 rats, vagotomized series 0 ulcers in 15 rats).

3 The duration of life of pylorus ligated rats was lengthened by vagotomy (control series forty six hours, vagotomized series ninety seven hours).

4 Neither the decrease in volume nor in acidity of the gastric fluid after vagotomy entirely explains the lack of ulceration in these rats.

5 In a series of thirty six clinical vagotomies, thirty four of which have been performed during the past nine months, there have been four failures of the operation (11 per cent).

6 The triad of symptom changes produced by the procedure in clinical cases includes relief of pain, relative diarrhea and delayed gastric emptying. The gastric distention occurred in one case entirely independently of any possible pyloric scarring or stenosis.

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effectively shown that such is not the case. It is intended to emphasize that in dealing with an entirely male population one should expect to see 60 per cent more peptic ulcers than one encounters in a hospital population which is of the same magnitude but made up half of men and half of women.

The revival, improvement, and practical application by Dragstedt¹³ and later by Moore and associates³⁶ of the operation of vagotomy first practiced for gastroduodenal disorders by Exner and Schwarzmunn in 1915,³⁰ Bircher in 1920,⁷ Lataret in 1921,³⁰ McCrea in 1925,³¹ Hughson in 1930,³⁶ Pieri in 1932,³⁸ and by Weinstein and co workers in 1944⁴² has offered new hope in decreasing this large amount of disability. It is the purpose of this paper to report our experiences with the results of the operation as applied to fifteen patients suffering from duodenal or stomal ulcer.

Selection of Cases—Table I shows the total surgical statistics relative to peptic ulcer for the six months July to December 1946 during which most of these operations were performed. It can be seen that more than one half the patients with duodenal ulcers operated upon during this period were subjected to vagotomy. Basing our criteria for operation largely on the recommendations of Dragstedt and of Moore and associates it was initially decided that we should accept for surgery only those patients who were young uncontrolled on medical therapy who had a high degree of stress sensitivity, a gastric secretion high in acid with a copious amount of night secretion and who presented no cicatricial pyloric obstruction. Made enthusiastic by the ability of this procedure to heal ulcers in our first few cases we shortly expanded the indications for vagotomy to include other patients who needed surgery for duodenal ulcer.

TABLE I SURGERY FOR PEPTIC ULCER JULY 1 1946 TO DEC 31 1946 AT THE VETERANS ADMINISTRATION HOSPITAL WEST ROXBURY MASS.

	DUODENAL ULCER	STOMAL ULCER	GASTRIC ULCER	TOTAL
Subtotal gastrectomy	7	1	6	14
	9	4		13
	1			1
	0			0
				1
Total peptic ulcers discharged				91

In order to adopt a consistent policy in our first cases we have considered the following as contraindications for inclusion in this series: (1) Recent massive hemorrhage in patients over 45 years or active bleeding at the time of surgery at any age; (2) diagnostic uncertainties produced by conflicting x rays such as whether the ulcer was on the gastric or duodenal side, unusual duodenal deformities or occasionally whether an ulcer was present at all; (3) obviously poor mechanical situations resulting from ill advised previous surgery such as a high anterior gastroenterostomy; and (4) pyloric obstruction. Under these criteria therefore there may be included for vagotomy some of those intractable cases in the middle aged group without copious night secretion and others with complicating factors such as chronic alcoholism, Buerger's

EXPERIENCES WITH VAGECTOMY FOR PEPTIC ULCER

WITH REPORT OF AN UNSUCCESSFUL CASE

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AMONG doctors in the Department of Medicine and Surgery of the Veterans Administration there is an impression that the incidence of peptic ulcer in veterans hospitals is high. This impression is borne out by the fact that the percentage of patients with peptic ulcer discharged from the West Roxbury Veterans Hospital during the first three years of its activity was 6.7 per cent, a figure considerably higher than the percentage incidence of the same condition among admissions to civilian hospitals. The highest figure that can be found in the literature for the incidence of peptic ulcer among admissions to a civilian hospital is that of 4 per cent as reported by Emery¹⁷ for the Peter Bent Brigham Hospital. Most other reported figures are much lower for example, that of Kauter¹⁸ who cited 0.77 per cent for Bellevue Hospital for the year 1941.

Although there are many possible explanations as to why the Veterans Administration should see and treat a large number of these patients, the most urgent one is the fact that the patients are predominantly male. Clinical statistics show that the frequency of peptic ulcers among men is four to five fold that in women.^{18, 19} A search for other reports which emanate from hospitals having essentially a male population brings to light that of Chamberlain²⁰ who gave a figure of approximately 2.79 per cent as the incidence of ulcer in a large army general hospital in the United States in war time. The logical explanation as to why the incidence in Chamberlain's male population should be lower than in ours is that the average age of a group of patients in an army hospital in war time is, by definition of the word veteran, younger than that in a veterans hospital. Emery and Monroe¹⁸ have stated that the average age at onset of peptic ulcer is 35 years. That the average age of a hospital population can on this basis alter the incidence figures is shown by the fact that the percentage of peptic ulcer among our patients in the first two and one half years of this survey was 7.4 per cent (624 ulcers in 8148 hospital discharges). During this time an average of 38.1 per cent of the hospital population was made up of veterans of World War I. For the last six months of the three-year period, when this figure rose to 57.0 per cent, the incidence of ulcer fell to 4.1 per cent (91 ulcers in 2,221 hospital discharges).

These considerations are not meant to infer that the incidence of ulcer is higher among soldiers than among civilians. Halsted²¹ and Tidy²² have

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TABLE II SUMMARY OF FIFTEEN PATIENTS RECEIVING VAGECTOMY AS THE ONLY PROCEDURE FOR DUODENAL OR STOMAL ULCER

POSTOPERATIVE X RAY										FINAL EMPTY ING		
ULCER NICHES SEEN	INITIAL EMPTYING	PERISTALSIS										
AGE	LOCATION OF ULCER	GROUP	STRESS SENSI- TIVITY	OPERA- TIVE APPROACH	DATE OF OPERA- TION	POSTOPERATIVE COMPLICATIONS	EARLY CLINICAL RESULT (1-6 MO)	Ulcer Niche Seen	Initial Emptying	Peristalsis	Final Empty- ing	
1	26	Duodenum	I	++++	Thoracic	6/29/46	Omitted twice	Moderate reten- tion, needs further surgery	No	Delayed	Normal	Delayed
2	21	Stoma	II	++++	Thoracic	7/15/46	Hemothorax	Dumping syn- drome not relieved	No	Rapid	Normal	Normal
3	44	Duodenum	I	++++	Thoracic	8/9/46	Bursitis	Moderate reten- tion, needs further surgery	No	Normal	Slightly decreased	Delayed
4	52	Stoma	II	++++	Thoracic	8/15/46	None	Excellent	No	Normal	Slightly decreased	Normal
5	27	Duodenum	I	++++	Thoracic	8/22/46	None	Excellent	No	Normal	Slightly decreased	Normal
6	29	Stoma	II	++	Thoracic	8/29/46	None	Excellent	No	Normal	Normal	Normal
7	40	Duodenum	I	++++	Thoracic	9/10/46	None	Excellent	No	Normal	Slightly decreased	Delayed
8	51	Duodenum	I	+++	Thoracic	9/13/46	Omitted twice	Excellent	No	Normal	Normal	Delayed
9	33	Duodenum	I	++++	Thoracic	9/24/46	None	Excellent	No	Normal	Normal	Normal
10	27	Stoma	II	+	Abdomi- nal	10/25/46	None	Excellent	No	Normal	Normal	Normal
11	42	Duodenum	III	0	Thoracic	11/5/46	Gastric reten- tion, two gas- tric ulcers	Failure gastric resection per- formed	Unsatis- factory	Delayed	Normal	Delayed
12	34	Duodenum	I	+++	Thoracic	11/22/46	None	Excellent	No	Normal	Slightly decreased	Delayed
13	24	Duodenum	I	++++	Thoracic	12/7/46	None	Excellent	No	Delayed	Normal	Delayed
14	50	Duodenum	III	0	Thoracic	12/10/46	None	Excellent	No	Normal	Normal	Delayed
15	46	Duodenum	I	++++	Thoracic	12/30/46	None	Excellent	No	Normal	Slightly decreased	Slightly delayed

disease and psychoneurosis. Such patients fall in the group so well described by Allen,¹ who said, "Some of them may be aided by the psychiatrist, while others are actually not willing to help themselves or do not possess the intellect to carry on their job and take care of their malady."

For purposes of study we have arbitrarily placed our patients in three groups. The first two groups were from the reports of others considered to be favorable, Group I being the young patients with hypersecretion, Group II being the patients with stomal ulcer following an earlier gastrojejunal anastomosis. Group III is the theoretically less favorable group mentioned previously. Although two patients in addition to these fifteen underwent vagectomy, they had a simultaneous gastroenterostomy for pyloric obstruction and, therefore, are not included in the series. From fear of mistaking a carcinoma for an ulcer no patient with a gastric ulcer was operated upon by vagectomy with the exception of one who had a stomal ulcer which appeared to be slightly on the gastric side of the stoma. This had nearly healed on medical treatment before the vagectomy was performed.

Technique of Operation—The transthoracic route was used in all but one case. Moore's modification of Dragstedt's² technique was employed. The thorax was entered through the perosteal bed of the eighth rib, the mediastinum opened and through the esophageal hiatus of the diaphragm both vagi were divided at a point 2 cm. below the cardiac orifice of the stomach. They were mobilized up to a point more than halfway between the diaphragm and the lung root, a 2 cm. segment of each nerve was resected and the proximal cut ends were incarcerated together in a silk cylinder which was sutured intrapleurally with the ends pointing upward. Reinspection of the esophagus was then performed to make certain that a 5 cm. circumferential segment just above the diaphragm was completely free of additional longitudinal nerve filaments of which there were often three or four. Transdiaphragmatic invasion of the peritoneal cavity as advocated by Moore was abandoned after the first two cases since it did not seem to afford any additional necessary exposure. Local procaine was used in the region of the nerves before mobilization in most cases.

In one patient of this group and in two additional patients who because of associated procedures were not included the transabdominal route was used. In these three the technique of Dragstedt was used with the addition that in two of them the nerve ends were incarcerated in a silk cylinder as in the transthoracic operation.

Early Complications—There was one patient who developed minor atelectasis. One patient developed contralateral pneumothorax and mediastinal emphysema. Ten had a considerable amount of postoperative hyperpyrexia amounting to 101° to 102° F. for three or four days. Most had annoying postoperative chest pain. One developed subdeltoid bursitis. Three patients developed symptomatic postoperative gastric retention. Two of these consisted of one episode of vomiting. The third suffered exacerbation of a duodenal ulcer and developed two gastric ulcers in addition. One of the patients not included in this series developed periarteritis nodosa in the early postoperative course.

TABLE IV COMPARISON OF TWELVE HOUR NIGHT SECRETION BEFORE VAGECTOMY WITH THAT IN THE LATER POSTOPERATIVE PERIOD (OVER TWO MONTHS) IN FIVE PATIENTS FOLLOWING VAGECTOMY*

PREOPERATIVE C.C.	POSTOPERATIVE C.C.
1350	800
1300	850
1300	900
1100	750
1510	475
Average 1312 cc	795 cc

*In no case was a gastrojejunostomy present

TABLE V COMPARISON OF TITRATABLE FREE ACIDITY BEFORE VAGECTOMY WITH THAT IN THE EARLY POSTOPERATIVE PERIOD (UNDER FOURTEEN DAYS) AFTER VAGECTOMY IN THIRTEEN PATIENTS

PREOPERATIVE UNITS OF FREE ACID	POSTOPERATIVE UNITS OF FREE ACID
44	36
50	0
74	16
42	0
15	22
31	0
33	11
21	21
60	13
0	0
20	40
75	7
40	25
23	0
50	40
Average 43.7 units	22.6 units

TABLE VI COMPARISON OF THE FASTING FREE ACIDITY IN THE GASTRIC JUICE BEFORE VAGECTOMY WITH THAT IN THE LATER POSTOPERATIVE PERIOD (OVER TWO MONTHS) IN FIVE PATIENTS FOLLOWING VAGECTOMY*

PREOPERATIVE UNITS OF FREE ACID	POSTOPERATIVE UNITS OF FREE ACID
19	12
21	0
60	51
44	10
33	0
Average 33.4 units	14.6 units

*In no case was a gastrojejunostomy present

The character of the gastric residual was of interest. On aspirating the stomach in the morning following an overnight fast characteristically there were collected 100 to 200 cc of residual fluid containing a suspension of particulate matter, vegetable fibers, fruit husks and other solids which could be recognized as material ingested as long as three days before.

Information with regard to the motility of the stomach was derived wholly from x ray observation of the barium meal. In the fasting stomach a fluid level was often seen by fluoroscopy. As a rule the initial barium left the stomach within less than two minutes but the stomach did not empty completely for twenty four hours (Fig 1). Peristalsis seemed active, occasionally not so much as in the normal but was never completely absent.*

*I wish to acknowledge the assistance of Dr Egon Wisting who performed the x ray examinations.

and died of that disease nine months after vagectomy. No etiological relationship between the ulcer or the operation and the fatal disease could be established either clinically or at post mortem examination.

Results of Operation—Results of the operation are shown in Table II. All but three of the fourteen patients who have been recently examined after having recovered from the complications just described are clinically well one to eight months postoperatively. One of these is the patient who developed a flare-up of the duodenal ulcer and two additional gastric ulcers. He came to gastric resection seven weeks after vagectomy. The postoperative course following this was uneventful. The other two patients are suffering from gastric retention manifested by vomiting once or twice a week six months after vagectomy. They have been advised to undergo gastroenterostomy and will do so as soon as they can take time off from their work.

Postoperative x ray examinations both within ten days and in certain cases four to five months postoperatively have shown, with two exceptions, no ulcer craters remaining. The deformity of a 'duodenal cap' does not disappear. All the stomal ulcers have healed. The two exceptions are the patient who came to gastric resection and another whose ulcer crater was much smaller but two weeks postoperatively had not healed. A later examination is not available.

All patients have in the later postoperative period shown an increased appetite and ability to hold or to gain weight.

Effect on Gastric Secretion and Motility—Tables III, IV, V, and VI give the gastric acidity and volume of night secretion before operation and in the early and later postoperative periods. In the routine clinical performance of these tests a large margin of error is to be expected due to regurgitation of duodenal juice, swallowing of saliva or failure of proper functioning of the tube. This latter consideration is more serious in patients following vagectomy because of the retention in the stomach of particulate matter which is difficult to evacuate through any tube. Figures derived from these tests may however be taken to reflect trends since they seem to be comparably consistent in different patients. In general the volume of night secretion and the acidity were decreased postoperatively as has been described by Dragstedt.

TABLE III. COMPARISON OF TWELVE HOUR NIGHT SECRETION BEFORE VAGECTOMY WITH THAT IN THE EARLY POSTOPERATIVE PERIOD (FOURTEEN DAYS) IN THIRTEEN PATIENTS

PREOPERATIVE C.C.	POSTOPERATIVE C.C.
1100	450
1900	520
1500	400
1,350	1000
900	100
1540	550
1300	900
1300	1000
450	50
400	400
1000	50
350	300
1,550	150
Average 1184 cc	500 cc

DISCUSSION

Selection of Cases—It might be argued that the stated indications for vagectomy could be expanded in two respects. In the first place if the operation of vagectomy will heal duodenal ulcers so rapidly in other patients, will it not also do so in the older group who have recently bled? It has seemed to us that in view of the higher mortality² in the older group of massive bleeders a recurrence of hemorrhage could easily cause serious trouble before the ulcer was able to heal. Second why not include the patients with pyloric obstruction and perform a concomitant gastroenterostomy as recommended by Dragstedt¹²? This is a debatable point. When the operation of vagectomy can be considered as no longer on trial this is a logical next step. Until that time it has seemed to us unwise to combine an operation which is on trial with one which as a routine treatment of duodenal ulcer, has been found to carry an incidence of jejunal ulcer of about 10 per cent.^{3 16 22 23}

Technique—With regard to the technique of operation two points should be made. The first is as McCrea has shown that the anatomy of the vagus nerves in the region of the lower esophagus is not that of two isolated longitudinal nerve trunks. The esophageal plexus makes complete resection of all fibers above a level about 5 cm. above the diaphragm nearly impossible. For complete resection of the anterior and posterior vagus trunk therefore, attention is best directed to the lower 5 cm. of the esophagus. The second point is that unless there are contraindications to the transthoracic route such as the necessity for adequate exploration of the duodenum either in a new case to determine the character of the lesion or in a patient who has had a gastric resection to determine the presence or absence of a noxious antral remnant^{2 22} adequate resection by this route is technically somewhat easier and in our opinion is to be preferred.*

Complications—Most of the complications we have experienced have been described by Grimson and associates²³. Most of them have left no residual and have not affected the final result. Exceptions are the patients who developed gastric ulcers and the other not in this series who developed periarteritis nodosa.

We have no trouble with bradycardia or cardiac standstill as reported by Moore and co workers²⁶ and by Weeks and associates⁴¹. We have taken continuous electrocardiograms during vigorous manipulation of the vagi which have had no novocain injected in them. These have shown no alteration in the tracings. In view of the fact however that there is evidence from work on animals⁹ that stimulation of the vagi distal to the lung roots will cause bradycardia we have not used this as sufficient evidence to omit routine procaine infiltration of the nerves.

A

B



C

D

FIG. 1.—Barium meal performed twelve days following transthoracic vagotomy. A, 10 minutes; B, 1 hour; C, 4 hours; D, 4 hours following ingestion. Note barium in duodenum in A and in jejunum in B. Normal peristaltic waves in A and B, decreased waves in C and D and normal gastric tonus.

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performed. The patient did very well for three weeks postoperatively. On November 16 there were 40 clinical units of free acid in the fasting secretion. One hour after the subcutaneous injection of 20 units of crystalline insulin this value was 3.5 clinical units of free acid. The blood sugar one hour after insulin was 33 mg per 100 cc. Three weeks after operation the patient began to have epigastric pain with occasional vomiting. The pain became worse. One December 13 x-ray examination showed 80 per cent of a barium meal to be retained after twenty-four hours. No gastric ulcers were seen. The duodenum could not be visualized. On December 17 a subtotal gastric resection with a posterior Hofmeister end to side gastrojejunostomy was performed. Following this, until discharge one month later the convalescence was uneventful.

Pathologic Examination—Examination of the stomach showed two gastric ulcers, one chronic and one acute (Fig. 2). There was no evidence of disease of the arteries included in the specimen.

To our knowledge this is the second reported case in which the ulcer has become worse following vagectomy, the first being that of Weeks, Ryan, and Van Hoy.⁴¹ Our patient was in Group III because of Buerger's disease and mild addiction to alcohol. Postoperatively our apprehensions were realized when it was discovered that in spite of the evidence of adequate vagus interruption afforded by the insulin test the fasting acidity was higher than before operation. Further data with regard to the altered gastric physiology are not available in this case because the clinical course did not permit them. Speculation as to what may have occurred is of interest.

The effect of vagectomy on gastric function has been epitomized by McSwiney³⁹ as a general decrease in all functions of that organ. With minor exceptions this is supported by all experimental evidence on animals and clinical evidence in man.^{13 21 22 23 26 30 31 33 34 36 38} There have been conflicting opinions as to whether pylorospasm is present or not. In general, although Lixner and Schwarzmann²⁶ and Kle²⁹ mentioned pylorospasm it is possible that they may be using the word interchangeably with gastric retention, which is a different thing. Many^{21 26 41 42} have noticed a decreased initial emptying time (a more rapid appearance of the initial barium in the duodenum). We have not observed this to be more rapid but merely not delayed. The presence of peristalsis such as we have observed is compatible with the result of sympathetic activity. McCrea spoke of the "postural tonus" afforded the stomach through the thoracolumbar outflow. The retention of solid food and the ready passage onward of liquid food has been well described by Ferguson²¹ from observation on monkeys. All the evidence in our patients the retention of particulate matter, the failure to find at any time a large intragastric volume of fluid and the lack of clinical evidence of pyloric obstruction corroborate this situation of which pylorospasm is not a part. The presence of normal peristalsis makes one wonder why the particulate matter does not pass along. Normal propulsive forces in the gastroduodenal segment may be defective even in the presence of active visible peristalsis.^{*} Perhaps the lack of flushing or lubricating secretion hinders the emulsion and passage of the particulate matter from the stomach. Might the favorable action of gastroenterostomy on postvagotomy gastric retention be due more to the duodenal secretions which this operation

supplies to the stomach than to the added size of the total available gastric outlet!

In the light of these considerations it is proper to speculate why vagectomy might make the occasional patient worse. It has been shown that vagectomy will cause gastric ulcers almost routinely in the rabbit⁴ and occasionally in the dog⁵ and monkey.²¹ In light of the recent interest in vagectomy the importance of the cephalic phase of gastric secretion has been greatly emphasized. It is logical to suppose, however, that there are patients with peptic ulcer whose hyperacidity is the result of the activity of the gastric phase of gastric secretion.^{13, 27} Neutralizing factors in patients with hypersecretion are the gastric mucus^{8, 27} and the regurgitated alkaline duodenal juice.^{8, 27} Although Ferguson¹¹ has shown that there is some mucus still present in the juice of a vagectomized stomach, Babkin³ has demonstrated that the "vagus juice" is moderately rich in mucus whereas the "histamine juice" has little. It is undeniably possible that in certain ulcer patients the gastric phase of secretion contributes more to the hyperacidity than the cephalic phase. In these patients removal of some of the alkaline mucus by vagectomy, especially if there were enough pyloric obstruction to prevent duodenal regurgitation, might render the gastric mucosa more vulnerable to ulceration.

It is our impression that in spite of the complications mentioned and the one unfavorable result reported, vagectomy has opened a new era in the surgery of peptic ulcer and promises to decrease greatly the disability caused by that disease. It seems probable, however, that there will continue to be certain patients in whom the operation may not be beneficial and in whom subtotal gastrectomy will remain the operation of choice. These patients, it seems, will fall more in clinical Group III than in either of the other two clinical groups described. Great caution should be exercised and careful gastric secretion studies performed before subjecting patients from this group to vagectomy.

SUMMARY

1 The incidence of peptic ulcers in the Veterans Administration Hospital, West Roxbury, over a three year period was 6.7 per cent. This figure is considerably higher than those reported from other hospitals.

2 A probable explanation for this is an exclusively male hospital population.

3 Early results with the operation of vagectomy in fifteen patients have offered hope of decreasing this large amount of disability among veterans.

4 The action of vagectomy on gastric physiology appears to be that of decreasing all the functions of the stomach. It does not cause pylorospasm. The retention of solid material and the passage of liquids is the result of this action. In most cases it causes no symptoms.

5 One patient is reported who developed two gastric ulcers following vagectomy for duodenal ulcer and required gastric resection. A theoretical explanation for this is offered.

6 Recommendations for the selection of patients for vagectomy are made.

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supplies to the stomach than to the added size of the total available gastric out-let?

In the light of these considerations it is proper to speculate why vagectomy might make the occasional patient worse. It has been shown that vagectomy will cause gastric ulcers almost routinely in the rabbit⁴ and occasionally in the dog⁵ and monkey.²¹ In light of the recent interest in vagectomy the importance of the cephalic phase of gastric secretion has been greatly emphasized. It is logical to suppose, however, that there are patients with peptic ulcer whose hyperacidity is the result of the activity of the gastric phase of gastric secretion.^{14,2} Neutralizing factors in patients with hypersecretion are the gastric mucus^{4,22} and the regurgitated alkaline duodenal juice.^{4,23} Although Ferguson⁴ has shown that there is some mucus still present in the juice of a vagectomized stomach, Babkin² has demonstrated that the "vagus juice" is moderately rich in mucus whereas the "histamine juice" has little. It is undeniably possible that in certain ulcer patients the gastric phase of secretion contributes more to the hyperacidity than the cephalic phase. In these patients removal of some of the alkaline mucus by vagectomy, especially if there were enough pyloric obstruction to prevent duodenal regurgitation might render the gastric mucosa more vulnerable to ulceration.

It is our impression that in spite of the complications mentioned and the one unfavorable result reported, vagectomy has opened a new era in the surgery of peptic ulcer and promises to decrease greatly the disability caused by that disease. It seems probable, however, that there will continue to be certain patients in whom the operation may not be beneficial and in whom subtotal gastrectomy will remain the operation of choice. These patients it seems, will fall more in clinical Group III than in either of the other two clinical groups described. Great caution should be exercised and careful gastric secretion studies performed before subjecting patients from this group to vagectomy.

SUMMARY

1 The incidence of peptic ulcers in the Veterans Administration Hospital West Roxbury over a three-year period was 67 per cent. This figure is considerably higher than those reported from other hospitals.

2 A probable explanation for this is an exclusively male hospital population.

3 Early results with the operation of vagectomy in fifteen patients have offered hope of decreasing this large amount of disability among veterans.

4 The action of vagectomy on gastric physiology appears to be that of decreasing all the functions of the stomach. It does not cause pylorospasm. The retention of solid material and the passage of liquids is the result of this action. In most cases it causes no symptoms.

5 One patient is reported who developed two gastric ulcers following vagectomy for duodenal ulcer and required gastric resection. A theoretical explanation for this is offered.

6 Recommendations for the selection of patients for vagectomy are made.

LOCALIZED ACQUIRED MEGACOLON TREATED BY SYMPATHECTOMY

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MEGACOLON may be encountered in any age group, two distinct varieties being recognizable. The first is true megacolon, or Hirschsprung's disease, occurring in infants and children and considered to be a congenital dilatation of the colon of neurogenic origin. The second type is acquired megacolon, or pseudomegacolon, occurring in adults and usually described as secondary to chronic colonic obstruction^{1, 2} from elongation of the mesentery, redundancy of mucosal valves, obstructing bands, rectal stricture, and rectosigmoid tumors³. That acquired megacolon may occur in the absence of demonstrable organic obstructive lesions is attested by the cases herein reported.

Hirschsprung's disease has been treated successfully in many instances by some form of sympathetic denervation of the colon. Both unilateral (Wade and Royle⁴) and bilateral (Judd and Adson⁵) lumbar ganglionectomy were employed during the earlier phases of the development of denervation therapy. Later, combined presacral, para-aortic and inferior mesenteric sympathetic plexus resection was introduced by Rankin and Learmonth^{6, 7}. Still later, Adson⁸ increased the extent of these procedures to combine not only bilateral lumbar trunk resection and presacral neurectomy but also bilateral lumbar sympathectomy and splanchnic nerve resection in patients having involvement of the entire colon. Penick⁹ has reported within the past year successful results from unilateral (left) lumbar ganglionectomy in a series of patients some of whom had a severe form of megacolon.

Recently Grimson and his associates^{9, 10} have presented data indicating that segmental or total colectomy may be preferable to sympathectomy in the treatment of neurogenic megacolon. This is supported by Yeazell and Bell¹¹ and by Whitehouse, Borgen, and Dixon,¹² being based upon accumulating reports of complications (volvulus, impaction and perforation) after sympathectomy. Grimson and his co-workers^{9, 10} have expressed the opinion that sympathetic denervation of the colon may be harmful in that the resulting interruption of visceral pain pathways deprives the patient of the ability to recognize the impending danger of impaction and perforation. Cattell and Colcock¹³ advocated resection, but combined segmental resection with sympathectomy in two cases. Herrmann¹⁴ advised lumbar ganglionectomy along with the Rankin-Learmonth procedure. He also advised resection in advanced cases.

Regarding therapy in acquired megacolon of adults, or pseudomegacolon, removal of the underlying cause represents, theoretically, the method of choice. However, when anatomic factors which are not readily amenable to direct

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months after operation. For about one year before death, increasing evidences of senile decay had been present, characterized by tremulousness especially of the upper extremities. For six months, constipation had again become a problem. For three weeks, incontinence of urine had been present. Four days before death, fresh bleeding from the rectum occurred for the first time. There was also a cough productive of mucus and blood. A small amount of barium by rectum showed again a local segmental dilatation of the rectosigmoid. Necropsy was not obtained and the origin of the bleeding was not determined.



Fig 1 (Case 1)—Segmental dilatation confined to a sigmoid colon

Comment—Beyond all doubt this patient represents a case of acquired megacolon with onset late in life without demonstrable cause of the sigmoid distention. Such pseudomegacolon has been considered usually secondary to

surgical attack are encountered or when no demonstrable causative lesion is found, there remains a choice of either sympathectomy or some form of colonic defunctionalization or resection. Martin and Burden¹² believed that hypertonus of the rectosigmoid sphincter can cause megacolon in the adult. Rankin and Learmonth⁶ reported the case of a 23 year old woman relieved of 'rectal obstipation' after pre-sacral neurectomy. Trumble¹³ stated that good results followed sympathectomy in various types of colonic dilatation in the adult but did not report specific cases. In other papers the occurrence of acquired megacolon is mentioned without further detail. It seems, therefore, of interest to report here three cases of acquired idiopathic megacolon treated by sympathectomy.

CASE REPORTS

CASE 1 (Roper Hospital No 6205)—A 71 year old white man had progressive constipation of one year's duration. He had led an active life with normal bowel habits until the present illness. For several years there had been some decline in strength with tremor of the lower extremities, which required him to give up his favorite sport of golf. His difficulty began with the passage of hard stools which were noted to be of smaller diameter than normal. Laxatives were used freely. On occasion large amounts of gas were expelled along with small pellets of feces. Some of the stools were of pencil-sized caliber while others were of normal size. There had been no diarrhea. Some intermittent distention with a feeling of fullness in the left lower quadrant had occurred without nausea or vomiting. No bloody or tarry stools had been noted. Anorexia developed with a weight loss of seventeen pounds during the year.

X-ray examination, done elsewhere, after oral barium demonstrated a local dilatation of the sigmoid colon apparently due to an obstructive lesion (Fig 1). This examination

ere not available.

General physical

Lower abdomen and

tenderness in the left lower quadrant. No masses were palpable abdominally or rectally. A tentative diagnosis was made of carcinoma of the lower sigmoid colon. He was placed on a preoperative regime of low residue diet with vitamin supplements and enteral chemotherapy at home and for five days before operation in the hospital.

Laparotomy through a left lower rectus incision was performed under low spinal anesthesia. On opening the abdomen a greatly distended segment of sigmoid colon was encountered (Fig 2) with rectosigmoid of normal caliber below. Palpation revealed no mass or other cause of obstruction. There was no volvulus. While the sigmoid seemed somewhat redundant and elongated, it was not of the proportions of a dolichocolon. The wall of the dilated portion was thickened. The bowel proximal to this was normal.

The posterior peritoneum was incised from the inferior border of the sacral promontory up above the origin of the inferior mesenteric artery. A block dissection of the superior hypogastric, inferior mesenteric, and preaortic plexuses was done. All loose tissue about the inferior mesenteric artery was carefully excised to insure complete denervation. Immediately on section of the presacral nerves, the distended segment of sigmoid colon began to contract vigorously. Within a few seconds it had returned to a size smaller than normal due to continuous hyperactive peristalsis.

Postoperative recovery was prompt with normal bowel movements beginning on the third day. On the fourth day, two small internal hemorrhoids prolapsed. They were excised under local anesthesia beyond transfixion sutures. The patient went home on the eleventh day and walked up to the second floor of his home. He continued to have satisfactory bowel function for over four years with only occasional use of cathartics. At the age of 76 years death occurred in a private sanatorium, rather suddenly four years and eight

Physical examination revealed a poorly nourished white woman whose facial expression was apprehensive and who was breathing rapidly and with apparent difficulty. Blood pressure was 120/70, pulse 110, respirations 38, and temperature 98.4° F. There was marked abdominal distention which was symmetrical and generalized. Palpation revealed a tense abdominal wall but no frank rigidity. The percussion note was tympanitic throughout the abdomen and flanks. On auscultation, great bursts of peristaltic activity were heard, accompanied by numerous high pitched metallic tinkles. There was evidence of bilateral elevation of the diaphragm with compression of the base of each lung field posteriorly. There were no other findings of significance. Routine laboratory studies were normal except for a moderate hypochromic microcytic anemia.

On the day after admission, the patient passed spontaneously tremendous quantities of gas by rectum and the distention subsided almost completely. Examination at that time



Fig. 3 (Case 2).—Well defined generalized dilatation of the large bowel.

a pathologic or anatomic factor producing chronic obstruction. It, therefore, is seldom mentioned in connection with sympathectomy, its treatment depending upon the usually demonstrable causative agent. That inferior mesenteric and presacral neurectomy may favorably influence acquired sigmoid megacolon is graphically illustrated in this case. The contractions of the colon which occurred immediately after section of the presacral nerve represent the counterpart of the experimental colonic contractions produced in dogs by Learmonth and Markowitz¹² by resection of the lumbar colonic nerve and the immediate emptying of the lower bowel in congenital megacolon after spinal anesthesia.¹³



Fig. 2 (Case 1).—Operative findings: megacolon is sharply localized in sigmoid segment ending at region of recto-sigmoid junction.

CASE 2 (Royer Hospital No. 12807).—A 34-year-old white woman entered the hospital complaining of "gas on my stomach and shortness of breath." The illness began about six years prior to admission shortly after an uncomplicated delivery of a living child. It consisted primarily of recurrent episodes of severe abdominal distention accompanied by dyspnea and palpitation. The syndrome was aggravated by eating. Much apprehension was occasioned by the dyspnea and caused the patient to abstain from eating for long periods. Constipation was pronounced in degree. Laxatives were required daily. As a result of the chronicity of the illness, weakness and malaise developed and were associated with a weight loss of eighteen pounds. The past and family histories were noncontributory.

nerves was removed in toto, the dissection being carried cephalad beyond the origin of the inferior mesenteric artery. Upon completion of the neurectomy, there was no change in size of the colon and no increase in peristaltic activity. After removal of the appendix, the abdomen was closed in layers. Routine pathologic studies of the excised specimen confirmed the presence of nerve fibers and ganglia.

The postoperative course was uneventful except for considerable distention, which was regarded as due in part to paralytic ileus necessitating decompression by Miller Abbott intubation and parenteral prostigmine. The patient was taking a full diet without discomfort on the tenth postoperative day. By that time all distention had disappeared and she was discharged in good condition twelve days after operation. After leaving the hospital, the patient improved gradually gaining weight and remaining free of the preoperative bouts of distention. She was examined again recently, three years and eight months after operation, at which time she was considered cured.

Comment—Like the first patient (Case 1), this patient represents an acquired form of megacolon first manifesting itself when the patient was 28 years of age. Careful evaluation of the history revealed nothing to suggest the existence of colonic atonia in childhood.

Celiotomy was done principally because of the possibility of a cecal carcinoma. When an organic lesion was not found and there was no demonstrable cause of the distended colon the question arose as to the choice of operative procedure for the megacolon. In view of the extent of the colonic dilatation resection was not considered leaving sympathetic denervation as the only applicable procedure. Through the abdominal approach employed in this case the maximum extent of denervation compatible with the patient's general condition was resection of both lumbar ganglionated chains and block excision of the presacral preaortic and inferior mesenteric plexus. Adson² has stated that such a procedure is adequate in relieving the symptoms of Hirschsprung's disease involving the descending and sigmoid colon but is not completely effective when the ascending and right half of the transverse colon also are involved. He has recommended for the latter condition bilateral splanchnic nerve resection in conjunction with removal of the first and second lumbar ganglia on each side performed in two stages. In view of the transperitoneal approach selected in this case presacral and inferior mesenteric neurectomy was regarded as the procedure of choice and performed accordingly. Further denervation at subsequent stages to include the splanchnic nerves, celiac ganglia, and lumbar sympathetic trunks was contemplated if the patient failed to improve. Despite the theoretical inadequacy of the procedure employed, the patient has remained entirely free of symptoms for almost four years and is judged to be cured. Possibly dysfunction in the rectosigmoid region had been the cause of retrograde dilatation of the entire colon.

Worthy of emphasis is the fact that this patient presented a well defined megacolon which according to the history, began in adult life and which, on operative exploration was found to exist without demonstrable cause. It may be regarded therefore, as acquired megacolon of undetermined origin.

CASE 3 (Roper Hospital No. 34702)—A 67 year-old Negro man entered the hospital complaining of cramping abdominal pain and vomiting. The illness began six months prior to admission with intermittent cramping pain over both lower abdominal quadrants accom-

revealed only moderate distention, but intestinal "pattern" was clearly demonstrable along with a slight degree of visible peristalsis. Barium x rays of the colon revealed a well defined generalized colonic distention, most pronounced in the sigmoid colon (Fig 3). There was loss of haustration in the latter segment. Fluoroscopic studies afforded evidence of a questionable, but persistent, deformity of the cecum which could not be disregarded entirely. It was the radiologist's impression that the presence of an organic lesion of the cecum was a possibility in addition to the colonic distention.

Three diagnostic possibilities were entertained: pseudomegacolon of undetermined origin, deficiency of vitamin B₁₂ with colonic atonia, and possible carcinoma or granuloma of the cecum. The latter impression was based upon the radiologist's report and the lesion was thought to be coincidental, if present at all, to the other two. In view of this possibility, exploratory laparotomy was advised.

Preoperative preparation with esterl chemotherapy, transfusions, and vitamins was carried out for five days. Distention was combated primarily by enemas.

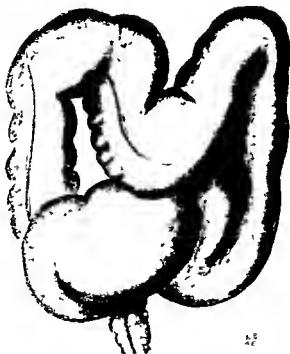


Fig 4 (Case 2) —Operative findings: note segmental loss of haustrations.

The abdomen was opened with the patient under inhalation anesthesia. There was no gross dilatation of the entire colon was present,

tion, there being no demonstrable organic or anatomic factors which would produce intestinal obstruction. The remaining abdominal viscera were normal. After division of the posterior peritoneum in the midline over the lumbosacral region, the presacral and preaortic plexus of

On the day of admission, a plain survey x ray view of the abdomen revealed gross distention of the entire colon with fluid levels. Fluoroscopic and radiographic studies were then carried out after administration of a barium enema, the enema tube being passed upward into the lower sigmoid colon. The latter filled without difficulty and was seen to be both elongated and greatly dilated. It formed a complete loop upon itself, the distal end of the loop overlying the lower portion of the descending colon (Fig 5). At this point, barium passed intermittently into the remainder of the large bowel as though an incomplete obstruction was present. It is to be noted in Fig 5 that there was distention of the colon both proximal and distal to the point of partial obstruction.

A diagnosis was made of sigmoid megacolon with partial obstruction probably due to adhesive bands. Because of the severe degree of colonic distention it was felt that a competent ileocecal valve was preventing retrograde decompression into the small intestine, thus creating the equivalent of a closed loop type of obstruction. Prompt decompression was considered necessary and a cecostomy was done under spinal anesthesia without exploration of the abdomen. The distention subsided slowly thereafter with gradual improvement in the patient's general condition.

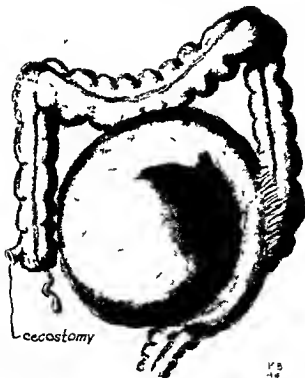


Fig. 6 (Case 3) —Operative findings thirty days after preliminary cecostomy, showing dilated sigmoid colon looped upon itself. Note adhesions between megacolon and descending colon.

Thirty days after the cecostomy, celiotomy was done under spinal anesthesia. There was a moderate increase in free peritoneal fluid. The sigmoid colon was enormously dilated (Fig 6), the dilatation extending downward into the upper rectal segment. A sharp line of demarcation was present between the distended sigmoid and the normal undistended descending colon. By looping upon itself, the dilated sigmoid formed a large knuckle of bowel the

panied by increasingly severe constipation. This was associated with recurrent episodes of abdominal distention and vomiting. Spontaneous remissions of the syndrome occurred after defecation, which was infrequent and prompted in each instance by vigorous catharsis. The recurrent bouts of distention became increasingly frequent in number. Anorexia developed progressively and there was a subsequent weight loss of twenty pounds. The stools were neither bloody nor tarry in character. The past history was normal, the patient stating that he had been in good health until the onset of the latter illness.

Physical examination revealed an elderly Negro man in obvious distress. There was moderate distention of the abdomen and the outline of the large bowel was clearly visible. There was no rigidity or spasm and no masses were palpable. Auscultation revealed that peristaltic activity was present but diminished. There were no other findings of significance.



Fig 5 (Case 3) —Barium filled sigmoid colon. markers indicate direction of the flow of barium from enema tube.

abdomen revealed a normal gas pattern. On recent examination two years and one month after operation, the patient at 70 years of age was found to be in good health. He had no complaints of abdominal discomfort. He had a good appetite and daily bowel movements without difficulty. Barium enema (Fig 7) showed an elongated sigmoid without dilatation or obstruction. There was some delay in passage of barium from the sigmoid into the descending colon at the point of previous adhesions but no dilatation of the descending colon.

Comment—The history of this patient denotes no symptoms of abdominal discomfort prior to the illness described which began when the patient was 66 years old. In view of the findings at operation a diagnosis of acquired sigmoid megacolon with dolichocolon was justified. Elongation and redundancy of the sigmoid colon were present and may be factors in the etiology of the megacolon. However there was no evidence to suggest an obstructive process distal to the sigmoid megacolon. On the contrary, the loop of distended bowel was so situated as to compress partially the descending colon producing a partial obstruction at that point. Paradoxically, this case represents an acquired megacolon which was the cause of intestinal obstruction rather than the result thereof.

The anatomic configuration of the sigmoid megacolon was such that eventual occurrence of volvulus of the distended loop would seem likely. This is a relatively common complication of megacolon, Weeks¹⁹ having reported sixty three collected cases and one of his own in 1931. It is likely that fixation of the megacolon to the descending colon by adhesions (Fig 6) prevented in some degree the occurrence of volvulus.

DISCUSSION

The operative procedure in these three cases may seem rather conservative but the results justified our limited operation. A thorough preaortic and presacral excision would seem to fulfill the requirements of an adequate postganglionic neurectomy for the distal colon. While we have found it feasible to remove the third and fourth lumbar ganglia in other types of cases by incision across the mesocolon it is ordinarily considered necessary to reflect the colon. This increases the magnitude of an operation begun as a transperitoneal exploration and in one case of congenital megacolon²⁰ was found to be technically impossible. The procedure used was without difficulty in all three cases. Resection was considered unnecessary in Case 1 and would have required staged operations in the others because of recent severe distention.

It is of interest to note that in all three cases bowel of normal caliber was present above the peritoneal reflection. The level of sharp transition from normal to dilated bowel inferiorly corresponded to the so called pelvicorectal sphincter of O'Brien.²¹ While the dolichocolon in Case 3 may have presented some opportunity for mechanical obstruction no such possibility was apparent in the other two. It would seem rather that a dysfunction of the order of an achalasia was the more likely cause.

While spinal anesthesia was not utilized therapeutically because the true condition was not recognized preoperatively it is of interest to note that in two patients (Cases 1 and 3) operated upon under spinal no apparent con-

medial border of which was in contact with the cecum, the lateral border being held firmly against the descending colon by numerous organized adhesions (Fig 6). Compression of the descending colon by the large knuckle of sigmoid colon was apparently responsible for a partial degree of obstruction. The remainder of the large bowel appeared normal. By sharp dissection, the adhesive bands were divided, thus freeing the dilated loop. A presacral neurectomy was done in the routine manner, the denervation being carried upward upon the aorta to the origin of the inferior mesenteric artery. There was no immediate change in the size of the dilated loop and peristalsis was not demonstrable after the neurectomy. The abdominal incision was closed in layers. Routine pathologic study of the removed tissue demonstrated the presence of nerve fibers and ganglia.



Fig 7 (Case 3)—Barium study two years one month postoperatively; redundant sigmoid is not notably dilated.

Recovery of the patient was uneventful. Normal bowel movements began on the sixth postoperative day and the cecostomy ceased to function after the tenth day. Two weeks after the operation, the patient was discharged much improved and free of distention. He has continued to remain comfortable and to have one normal bowel movement daily. There have occurred no more episodes of abdominal distention. Postoperative plain radiographs of the

MANAGEMENT OF CANCER OF THE COLON

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IT IS evident from a review of the recent literature that surgeons throughout the country are prone to employ different methods in the treatment of cancer of the colon. There is general agreement as to the amount of bowel and mesentery that needs to be removed, based upon careful anatomic studies of the regional lymphatic drainage and the blood supply to the parts. Attempt is always made to transect bowel at points wide of the primary growth, to remove an extensive area of the regional mesentery and its contained lymphatic structures, and to preserve blood supply to the remaining segments of the colon. To accomplish these ends plans of management have been established in most clinics which work well in the hands of surgeons in those clinics though they may differ considerably from methods used elsewhere. The differences of opinion among surgeons lie largely in the technique of resection and re-establishment of continuity of the bowel after resection. Two groups exist, comprising those who choose a method requiring delayed anastomosis and those who prefer to restore continuity of the intestine immediately.

Much progress along both lines of approach has been made since the cure of cancer of the colon began. In 1895 Paul¹ recorded seven cases of colectomy. Two of the first three patients died as a result of necrosis and leakage following resection and immediate anastomosis in the presence of complete obstruction. The remaining five were treated by resection and exteriorization of the loops of bowel. Three of these patients recovered, and Paul concluded that the latter procedure was the one of choice. The practice of exteriorization was then popularized by Mikulicz² and has been amended by Rankin³ and Lahey⁴ so that earlier objections to its use have been overcome.* These were the frequent implantation of cancer into the abdominal wall and the insufficient removal of regional mesentery and lymphatic structures. Important technical improvements which aid in the construction and closure of the colostomy have been described by these men and others, and have resulted in a refined management which has produced enviable results in operative mortality. Preference for this method of resection as opposed to primary anastomosis is given by Rankin,³ Lahey,⁴ Jones,⁵ Dixon,⁶ Fallis,⁷ and others.

The method of immediate anastomosis at the time of resection has developed and improved concomitantly. Koehler,⁸ in 1881, reported in some detail the first performance of resection with primary anastomosis crediting the operation to Professor H. Fischer of the Breslau University Surgical Clinic. The patient, a 33 year-old woman, suffered complete obstruction of the large bowel from a

Presented at the meeting of the Society of University Surgeons, Boston, Mass., Feb. 13, 1917.

*Paul resected the tumor at the time of exteriorization and inserted glass tubes into the open loops. Mikulicz left the tumor in place.

traction of the bowel was initiated by the anesthesia. In Case 1 immediate contraction of the dilated bowel followed neurectomy. Unfortunately in neither case was the exact level of analgesia during operation recorded, but it must have reached at least the tenth thoracic dermatome in both instances.

SUMMARY

Case reports are presented of three patients having acquired megacolon. In each the disease developed in adult life and in none was there a demonstrable causative factor. Each patient was subjected to a combined presacral, pre-aortic, and inferior mesenteric neurectomy.

One patient remained well for four years but died four years and eight months postoperatively. Two patients were well after three years and eight months and two years and one month, respectively.

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principles have remained about the same with only minor variations in pre operative and post operative care. It is our purpose to present the management in some detail and to report the operative results.

PREPARATION OF THE PATIENT FOR RESECTION

Once the diagnosis of carcinoma of the colon is made and the lesion is localized by sigmoidoscopy or roentgenology, the presence of constipation or obstipation, abdominal distention and x ray evidence of retention of gas, fecal material or barium indicates obstruction. In this clinic any degree of chronic or acute obstruction due to lesions situated distal to the hepatic flexure is relieved by antecedent proximal cecostomy or colostomy. Neither distended thin nor edematous thickened intestinal wall lends itself to safe anastomosis. Of equal importance is the fact that systemic disturbances secondary to obstruction militate against recovery. These may be disturbances in chemistry, nutrition and water balance and in mechanical interference with the respiration due to abdominal distention. Tangential cecostomy is preferred in cases of simple obstruction because it provides adequate decompression, it is safely and easily performed under local anesthesia in one stage and in most instances closure is spontaneous. If operative closure is required it is a relatively simple procedure. If associated local inflammation is present complete diversion of the fecal content as well as decompression is essential. Fever, leucocytosis, tenderness, palpable fixation and fistulous tract formation are signs of inflammation. When these are present in connection with lesions at or distal to the splenic flexure a modification of the Devine colostomy performed on the right or left half of the transverse colon is used. The technique for this and the method for later closure are as described by Ochsner, DeBakey and Rothschild.²¹

Obstruction secondary to lesions in the cecum and ascending colon is rarely encountered. This is due to the fungating quality of the growths with less tendency to scirrhus contracture, the larger lumen of the bowel and the fluid consistency of its contents. If obstruction is present here it often denotes incurability by resection because of either local extension of the tumor or wide spread metastases. Signs of associated local inflammation are also frequently present. Often the relief of obstruction in the right colon may be accomplished by use of the Miller Abbott tube or continuous gastric suction and frequent small enemas. Unless distinct progress is made in two or three days decompression is then best obtained by performing an ileotransverse colostomy through a short transverse incision. In our hands simple antiperistaltic side to side anastomosis has proved valuable. If the general condition of the patient and local condition of the bowel justify the procedure the ileum may be divided and the end turned in before the anastomosis is made.

In the absence of obstruction we do not hesitate to perform resection with immediate anastomosis without decompression. The pre-operative management of these cases and of those in which obstruction has been relieved is about the same. In the supportive management anemia is treated by adequate transfusion of whole blood and a diet high in carbohydrates, protein, and calories, and low

lesion in the descending colon just above the sigmoid. At the time of resection outpouring of fecal content occurred and trocar punctures were made to reduce small bowel distention. The union of the proximal and distal portions was effected with interrupted silk sutures as was the mesentery. The postoperative course was complicated by a fecal fistula occurring on the eighth day. This closed spontaneously and the patient was discharged in good health. Reichel⁹ reported that autopsy of this patient at death one year eleven months later revealed carcinomatous recurrence.

After this first attempt progress was delayed for some time, mainly because of reliance placed upon mucosal and serosal sutures, a frequent result being peritonitis due either to soiling occurring at the time of open anastomosis or to delayed leakage from separation of poorly united bowel ends. In 1910 Halsted¹⁰ basing his conclusions upon experiments performed on dogs, clearly demonstrated the importance of including the submucosal layer for added strength in the line of anastomosis. In addition he developed and described in well illustrated writings sound techniques for side to side and "aseptic end to end" anastomoses. Refinement in the one stage type of resection was then made by graduates of the Johns Hopkins school of surgery and by others. Techniques employed in this method for resection and reasons for preference, are described by such adherents as Stone and McLanahan¹¹ Cheever,¹² Allen,¹³ MacFee,¹⁴ Rankin¹⁵ (regarding right colon resections), Joll¹⁶ Gibbon and Hodge¹⁷ Whipple,¹⁷ Mayo¹⁸ Collier,¹⁹ Norton,²⁰ Waugh and Custer,²¹ and White and Amendola.²²

This alignment of surgeons indicates their choice as to primary or delayed anastomosis in the treatment of cancer of the colon in general, although deviations to the alternate method may be made in the presence of certain indications. Despite existing preferences there is no quarrel, and the mortality rates resulting from both lines of approach in the past twenty years have shown remarkable improvement. Proponents of each technique have reported numerous series of cases with low mortality rates and younger surgeons will continue to use the method in which they were trained in order to get the best results.

In the department of surgery of the University of Cincinnati the plan of choice has been that of anastomosis at the time of resection by either an open or a closed method. With this procedure it is necessary to establish suitable conditions for the relief of obstruction for the avoidance of sepsis and for primary healing by use of careful preoperative, operative, and postoperative measures. Immediate anastomosis is not suitable for those unwilling to be painstaking and to pay exact attention to details. If these conditions cannot be met in each individual case it is safer to resort to exteriorization and delayed anastomosis. It is our belief that they can be realized and that primary anastomosis is a safe method. Once safety is established, such considerations as greater postoperative comfort, freedom from annoyance of interval colostomy, relief from need for secondary operative procedures, and a shorter and less costly period of hospitalization become of importance to patients.

Under this plan eighty-seven resections for cancer of the colon have been performed in the nine year period from 1938 to 1946. During this time basic

arteries At the upper end of the field the descending portion of the duodenum is identified and the beginning of the transverse mesocolic reflection is divided at its attachment to the duodenum and to the anterior surface of the head of the pancreas The dissection below is carried proximal to the cecum to include the mesentery of about 12 cm of the terminal ileum, incising only the serosa The entire mobilized segment is then elevated and its blood supply visualized The points for division of the transverse colon above and the ileum below are selected, and the mesial reflection of mesentery is incised with a scalpel from these points to an apex at the points of origin of the right colic and ileocecal arteries The vessels are isolated, divided between clamps and transfixed with No 000 silk At the points selected for division of the transverse colon and the ileum the serosa is carefully cleansed of fat and mesenteric tissue by a gentle wiping process with a single layer of gauze over the finger Small perforating vessels are clamped close to the serosa as they are encountered, divided with a scalpel, and ligated with No 0000 silk This is done for a sufficient distance to permit the placing of clamps and for an additional margin of serosa to allow later in version or anastomosis without interposition of fat long segments of vessels, or large ligatures Pairs of Kocher clamps are applied in a position to shorten the antimesenteric borders of the visible segments The bowel is then divided with cautery at each site and the specimen is removed

At this point either a side to side anastomosis similar to the method of the Halsted enteroenterostomy²² or an end to side anastomosis somewhat according to the technique described by Rankin³ is employed If the side to side method is used simple closure of the ends of the ileum and transverse colon is made over the clamps with a single row of Halsted mattress sutures of No 000 silk These are laid in place to include the submucosa, drawn up to accomplish inversion as the clamp is withdrawn and tied The closure is then reinforced by placing a Lambert mattress suture between each two Halsted mattress sutures using No 0000 silk Another method often used is that of an inverting right angle (Cushing) suture of No 0 chromic catgut over the Kocher clamp This suture, after the clamp is removed and inversion is complete is continued back as a second row and tied We prefer either of these methods to that of ligating the bowel and inverting the ligated stump because they avoid cavities closed at each end with ligatures

After both ends of the bowel are closed the terminal ileum is held parallel to the longitudinal band of the transverse colon the field is carefully walled off with gauze packs and the side to side anastomosis is done near the ends in order to leave as little blind stump as possible Traction sutures of silk are placed at each end of the proposed anastomosis and a posterior continuous suture of No 000 silk is placed (Fig 1 1) Halsted mattress sutures of No 000 silk are then laid anteriorly (Fig 1 2) These are next pulled aside, half to each end (Fig 1 3) Before opening the bowel a temporary occlusion is produced to prevent gross soiling Rubber shoe clamps or soft lead bars (5 by 3 mm. in cross section and covered with soft rubber tubing) bent like a hairpin can be placed across the bowel One is used across the ileum and one across the colon

in residue is given. If the oral intake is not adequate, solutions of amino acids, glucose, and saline solution are used intravenously. Daily minimum vitamin requirements are satisfied.

In addition to the e

is given by rectum and through
is given orally each six hours \times \times days before operation. The dosage is calculated at the rate of about 0.25 Gm per kilogram of body weight for twenty-four hours. On the day before operation an x-ray examination is made for the presence of gas stool and barium in the colon. At this time the patient is placed on a liquid diet and continuous gastric suction is begun on the morning of operation.

On the day of operation the skin is shaved widely and prepared by gentle washing for five minutes with gauze saturated in 1:100 aqueous solution of ethylpyridinium chloride (ecephryn chloride). Towels and drapes are applied with regard to the planned location of the incision. All lesions of the colon except those lying very low in the sigmoid are approached through a transverse incision often extending into the flank as described by Hoag.¹⁴ We are convinced that the transverse incision affords better exposure than a vertical one; less retraction is required; wound disruption is encountered less often; there is less postoperative pain and splinting of respiration; and healing occurs with a finer scar. The wound is isolated from the skin by fixing the under sides of towels to skin edges with Michel clips. Careful attention is paid to hemostasis and the subcutaneous and muscular layers are protected from trauma and from the field of resection with moist laparotomy packs.

PROCEDURE FOR LESIONS IN THE CECUM, ASCENDING COLON, AND HEPATIC FLEXURE

Upon opening the peritoneum first the liver and then the regional lymphatic area are palpated for metastases. If remote metastases are present palliative resection may be done. Many of these patients remain in relative comfort for months. The primary growth is examined with care since rough handling may result in perforation and soiling. If there is evidence of an active inflammatory process extending beyond the bowel wall with or without abscess, ileocolostomy is done without resection. The differential diagnosis between appendiceal abscess, diverticulitis, tuberculosis, and infected tumor may be exceedingly difficult in such instances.

If this complication is not present the cecum, ascending colon, and hepatic flexure are mobilized by incising the avascular lateral mesenteric reflection. The bowel is rotated mesially and the ureter and spermatic or ovarian vessels are identified from their origin down to the brim of the pelvis and spared. The retroperitoneal fat and lymphatic-bearing tissue are removed using a gentle wiping process with gauze alternating with sharp dissection and carried mesially with the bowel and its mesentery to the points of origin of the right colic and ileocecal

tied, the anterior lip of the anastomosis is closed (Fig 2, 5). A Lembert suture of No 0000 silk is placed between each two mattress sutures. The angles of the anastomosis are reinforced with mattress sutures of No 000 silk and the occluding rubber shod clamps or lead bar clips are removed. After removal of the protecting gauze packs the gloves are changed before continuing the operation. The overlapping folds of the mesentery are sutured together to close the defect, care being taken not to injure the blood supply.

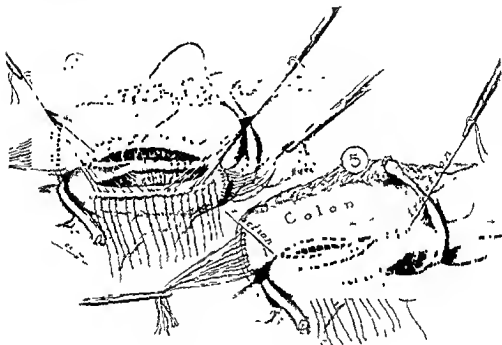


Fig 2-4 are in side to side colocolostomy (continued). (4) Posterior lock suture of catgut through all layers of bowel. (5) mattress sutures pulled up and tied. (From J Clin South America 23 1-12 1946)

If the end to side method of ileocolostomy is used, the cut end of the colon only is closed and a site is selected for the anastomosis. A portion is tented up by grasping it with two Allis clamps. A Kocher clamp is placed across this area longitudinally and the protruding portion, which is made to correspond in size with the diameter of the ileum, is excised with the cautery (Fig 3, 2). The stump of the ileum, which is held in a Kocher clamp, is then approximated to the defect in the colon and the anastomosis is begun. Using an atraumatic needle a posterior running suture of No 0 chrome catgut is placed with a tie at the beginning and a lock at the end, leaving both ends long in order to tie them later to each end of the anterior suture (Fig 3 3). The clamps are then rotated inward and a continuous right angle (Cushing) suture is placed anteriorly with no tie at either extremity (Fig 4, 4). The clamps are withdrawn as the assistant

At the site of the anastomosis itself no clamps are used. The bowel is held up by the assistant lifting the traction sutures and ordinarily there is no escape of intestinal contents. The bowel is opened with a knife and scissors or with high frequency cautery, and bleeding points are clamped and tied with No 000 chromic catgut, or they are coagulated (Fig 1 3). The posterior suture line is reinforced with a continuous lock stitch of No 0 or 00 chromic catgut which goes through the entire thickness of both walls (Fig 2 4). The ends of the anterior row of mattress sutures are pulled up, and the traction sutures are out or pulled aside, when the mattress sutures are drawn up to approximate the bowel and

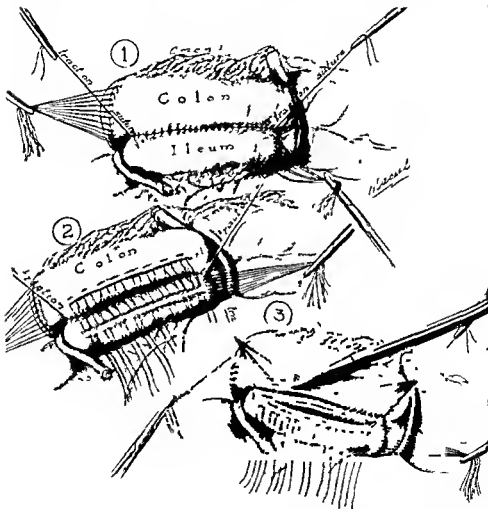


Fig 1—Steps in side-to-side ileocolostomy. (1) Posterior continuous sutures of silk between two traction sutures. (2) anterior row of Halsted mattress sutures placed. (3) mattress sutures pulled as de Hezels made in bowel and vessels clamped and tied with catgut or coagulated. (From S Clin North America 25 1201, 1946)

tion prevent the operator from proceeding with end to end anastomosis. Great disparity in the size of the bowel proximal and distal to the lesion may be present, requiring a side to side anastomosis in the manner just described for resection of the right colon. This may be true despite preliminary decompression and frequent irrigation. After careful exploration of the abdomen to determine the extent of metastases, adhesions adjacent to the lesion, led by sharp entry. The width of the mesentery, and the proposed sites for division carefully tested to determine that they

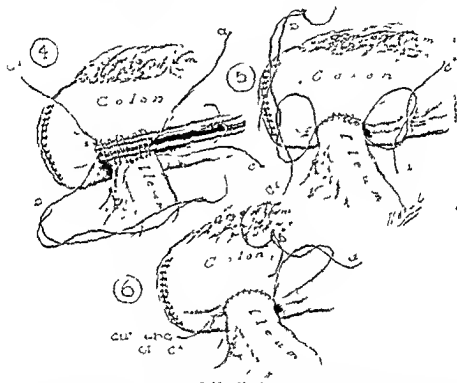


Fig. 4.—Steps in end to side ileocolostomy (continued). (4) Anterior right angle (Cushing) suture of cutgut over clamps. (5) anterior suture pulled up after clamps are removed. (6) posterior suture continued as second anterior layer. (From S. Clin. North America 25: 1204, 1946.)

can be approximated without tension. The lateral and mesial reflections of mesentery are divided from these points to an apex at the base of the mesentery. This is done with respect for blood supply and the vessels are ligated individually as described under the procedure for resections of the right colon. Extreme care is taken to remove the appendices epiploicae and other fat tabs from the bowel at the proposed site of anastomosis. The mesenteric clamps are applied diagonally on the mesenteric. A suture is placed through each Stone clamp, (Fig. 5, 1). The cut ends

makes traction on one end of the suture to begin the inversion. The operator completes the inversion by making traction on the other end of the anterior suture. Agglutination of the crushed ends of the bowel is depended upon to maintain closure until the inversion is accomplished. Corresponding ends of the anterior and posterior sutures are then tied (Fig. 4, 5). The long end of the posterior suture is continued around anteriorly and tied, forming a second anterior suture line (Fig. 4, 6). The continuity of the lumen is established by

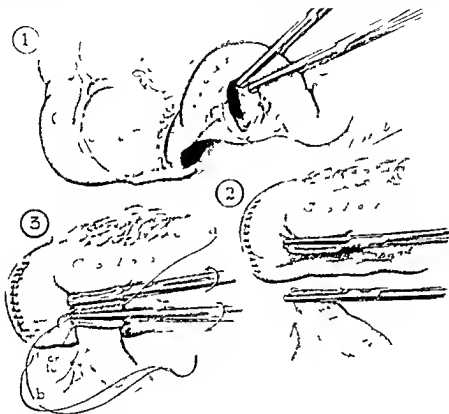


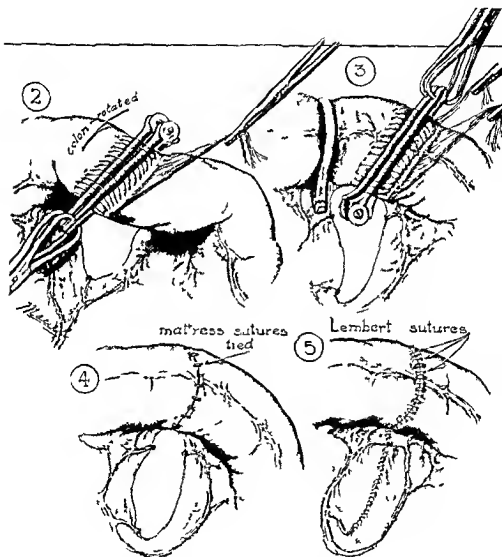
Fig. 3—Steps in end-to-ile ileocolostomy. (1) Dissection of terminal ileum. (2) Kocher clamp on side of colon. (3) posterior continuous suture of catgut. (from S. Clin. North America 23: 1-63, 1940)

invaginating the walls of the ileum and colon with the thumb and forefinger. The anastomosis is reinforced posteriorly and at the angles with Lambert sutures of No. 0000 silk. A portion of omentum is anchored loosely over the anastomosis with silk. The same attention is directed to the mesentery as described in the open type of anastomosis.

PROCEDURE FOR LESIONS DISTAL TO THE HEPATIC FLEXURE

For lesions beyond the hepatic flexure an end to end aseptic anastomosis is usually done, but in some cases circumstances encountered at the time of resec-

doubled No 000 black silk and the skin with interrupted No 0000 silk. In cases in which soiling has occurred the closure is usually made with 22 gauge silver or steel wire stay sutures which are placed through the entire thickness of the abdominal wall. No other sutures are used except for a few interrupted ones of fine silk in the skin to keep the edges of the wound from everting. The details of this method of wound closure are as described by Reid Zininger and Merrell²⁶



of the bowel held in Stone clamps are then brought into apposition. A single row of Halsted mattress sutures of No 000 silk is laid on one side just far enough from the clamps so that they can be pulled up and tied (Fig 6 2). A row of mattress sutures is laid on the opposite side of the bowel and a rubber shod clamp or lead clip is placed across the proximal loop (Fig 6 3). The Stone clamps are removed. The second row of mattress sutures is then pulled up and these are tied, completing the inversion (Fig 6 4). A Lembert suture of No 0000 silk is placed between each two Halsted sutures (Fig 6 5). Serosal approximation at the mesenteric border is the most difficult and must be obtained by precision in placing the sutures. After completing the suture continuity

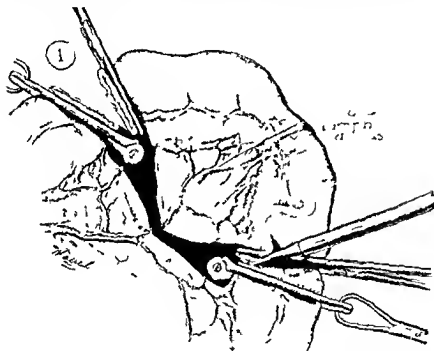


Fig —Steps in end to end anastomosis. (1) Division of bowel with cautery between Kocher and Stone clamps. (Fr in S Clin North America 22 1905 1916)

is established and the adequacy of the stoma is determined by invaginating the bowel on either side with the thumb and forefinger. The cut edges of the mesentery are approximated carefully to leave no defect or raw surfaces (Fig 6 5).

CLOSURE OF THE WOUND

The exact method of closure of the wound has differed with individual operators. As a rule the peritoneum is closed with continuous No 0 or No 1 chromic catgut. The wound is thoroughly but gently irrigated with saline solution. The muscle and fascia closed with interrupted figure of eight sutures of

doubled No 000 black silk, and the skin with interrupted No 0000 silk. In cases in which soiling has occurred the closure is usually made with 22 gauge silver or steel wire stay sutures which are placed through the entire thickness of the abdominal wall. No other sutures are used except for a few interrupted ones of fine silk in the skin to keep the edges of the wound from everting. The details of this method of wound closure are as described by Reid Zinniger, and Merrell²⁶

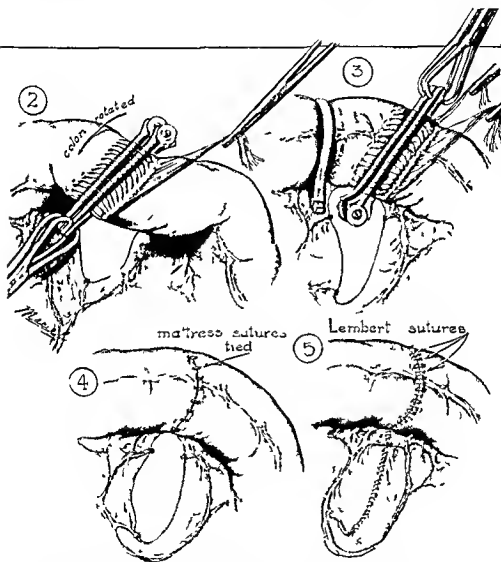


FIG. 6.—Steps in end-to-end aseptic anastomosis (continued). (2) Clamps rotated and first row of liaisted mattress sutures of silk placed. (3) first row of sutures tied and opposite row of mattress sutures placed. (4) Stone clamps removed and second row of mattress sutures tied. (5) completed anastomosis. (From S. Clin. North America, 1946)

POSTOPERATIVE CARE

The postoperative care is important but usually not difficult. The operation is not ordinarily accompanied by much loss of blood or by shock. Intravenous injection of glucose and saline solution is given during operation and whole blood is substituted if indicated. Sulfadiazine and penicillin are administered parenterally after operation if there is any question of sepsis having occurred or at the onset of signs of sepsis. We have abandoned the use of intra peritoneal implantation of sulfa drug for the past four years.

OPERATIVE DATA AND RESULTS

A total of 144 patients with cancer of the large bowel were seen of which 87 were treated by resection. At the Cincinnati General Hospital resection was accomplished in 45 out of 100 cases and with private patients in 42 out of 44. Since the same criteria for resectability were used in the two series the difference in operability seen in a private and charity clinic is vividly illustrated. The operability rate in the total group is shown in Table I. In the Cincinnati General Hospital the rate was 45 per cent while in the private service the rate was 90 per cent. It must be remembered that among private patients, one who is unquestionably inoperable may remain at home or on a medical service without surgical consultation. In a charity institution this situation is often reversed, a family or a family doctor sending the patient to the hospital to die. Of the 57 patients classed as inoperable 30 had no procedure because of marked advancement of the disease, 16 had palliative colostomies either internal or external and 11 had exploratory laparotomies without further procedure.

TABLE I. OPERABILITY RATE

	CASES	RESECTIONS	OPERABILITY (%)
Right colon	45	24	53.3
Transverse colon	22	16	72.7
Left colon	7	47	61.0
Total	144	87	60.4

Of the 87 resections performed 16 were classed as palliative having either lymphatic metastases beyond the limits of regional resection or liver or peritoneal metastases. In 4 instances resection of other organs was performed along with large bowel resection. These included resection of small intestine on two occasions, removal of the tail of the pancreas and spleen with a cancer of the splenic flexure and resection of a carcinomatous fistulous tract in the abdominal wall.

In lesions of the right colon ileotransverse colostomy as the first procedure was carried out twelve times, in ten of the cases however it was only palliative and was not followed by resection. In the other two cases resection was performed three and four weeks after the anastomosis. Only three of the twenty four patients with cancer of the right colon who had resection showed obstruction (see Table II). Of the sixty three resected for cancer of the transverse and left colon (see Table III) twenty nine or almost one half had complete or partial obstruction at the time of admission to the hospital. In all of these a cecostomy

TABLE II RIGHT COLECTOMY WITH ILEOTRANSVERSE COLOSTOMY

Cecum	10	End to side (one stage)	6
Ascending colon	3	Side to side (one stage)	16
Hepatic flexure	11	Side to side (two stage)	2
Total	24		24

or transverse colostomy was done to relieve the obstruction and the resection was done subsequently. Thirty four of the sixty three had resection without preliminary decompression.

In some cases of lesions beyond the hepatic flexure circumstances encountered at the time of resection prevented the operator from proceeding with end to end anastomosis. These occurred in only six out of sixty three cases in which resection was done. In four cases great disparity in the size of the bowel proximal and distal to the lesion necessitated side to side anastomosis in the manner just described for right colon resections. In two of the four cases a dilated proximal segment was present despite preliminary decompression by cecostomy and irrigations for thirty and sixteen days. No preliminary enterostomy had been done in the other two cases. In two cases Mikulicz obstructive resection was employed. In one of these the sigmoid colon proximal to the lesion was filled with inspissated stool despite antecedent cecostomy and seventeen days of attempts to cleanse the bowel by irrigation. In the other incision and drainage of an abdominal wall abscess secondary to perforation of the transverse colon at the site of the lesion was required at the time of admission to the hospital (see Table III).

TABLE III RESECTIONS TRANSVERSE AND LEFT COLON

Transverse	16	End to end	57
Splenic flexure	5	Side to side	4
Left colon	42	Mikulicz	2
Total	63		63

In the eighty seven cases of resection there were six deaths a mortality rate of 6.9 per cent as shown in Table IV. Four deaths were due to leakage at the site of anastomosis with peritonitis. All of these were in the left colon and three of the four were palliative resections with liver metastases. One patient died of pneumonia and one of uremia.

In order to compare these results with recent experiences of others the following operative mortality rates may be listed. Using the so called Mikulicz method Jones³ in 1943 reported a 6.5 per cent mortality in 77 resections and Luby⁴ in 1942 reported a 11.7 per cent mortality in 112 resections. In 1946 he

TABLE IV OPERATIVE MORTALITY IN CASES WITH RESECTION EQUALS 6 OF 87 CASES OR 6.9 PER CENT

	DEATHS	RESECTIONS	MORTALITY (%)
Cecum	1	10	10.0
Ascending colon	0	3	0.0
Hepatic flexure	0	11	0.0
Transverse colon	0	16	0.0
Splenic flexure	1	5	20.0
Sigmoid	4	42	9.5
Total	6	87	6.9

POSTOPERATIVE CARE

The postoperative care is important, but usually not difficult. The operation is not ordinarily accompanied by much loss of blood or by shock. Intravenous injection of glucose and saline solution is given during operation and whole blood is substituted if indicated. Sulfadiazine and penicillin are administered parenterally after operation if there is any question of sepsis having occurred or at the onset of signs of sepsis. We have abandoned the use of intra-peritoneal implantation of sulfa drug for the past four years.

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12 Parenteral administration of sulfadiazine and penicillin if soiling has occurred or at the onset of signs of sepsis

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reported another series with a 27 per cent mortality, the number of cases was not stated. Favoring the method of immediate anastomosis Stone and Mc Lanahan¹¹ in 1942 reported a 19.4 per cent mortality in 104 resections. Whipple in 1944 a mortality of 9.4 per cent in 117 cases, and Waugh and Custer¹ in 1945 a mortality of 4.0 per cent in 50 resections.

The average hospital period for the seventy nine surviving patients treated by resection and immediate anastomosis was twenty six days from resection to time of discharge from the hospital. In patients in whom a cecostomy was performed the average interval between the production of the cecostomy and resection was fifteen days.

SUMMARY

The method for treatment of cancer of the colon at the Cincinnati General Hospital has been presented. Resection and immediate anastomosis is preferred. The use of this method requires exact attention to details in preoperative operative and postoperative management, and has led to an operative mortality of 6.9 per cent. The series of patients operated upon presented here is small and is distributed over a period of nine years in a training school for young general surgeons. The resections were done by a number of surgeons many of whom were young residents in training. This indicates that good results may be obtained by any well trained general surgeon who occasionally operates on the colon for cancer providing he is taught and continues to observe the fundamental principles involved. These may be enumerated:

- 1 Preliminary correction of anemia and of disturbances in chemistry, nutrition and hydration
- 2 Relief of obstruction and attempts at thorough cleansing of the intestine before removal of the lesion
- 3 Use of the abdominal transverse incision
- 4 Careful attention during resection of the mesentery to preservation of blood supply to the segments of bowel at and adjacent to the proposed site of anastomosis
- 5 Gentleness in the dissection and handling of the bowel and its mesentery
- 6 Adequate mobilization of the segments to be anastomosed in order to prevent tension at the line of suture
- 7 Precision in placing of sutures after careful preparation of the bowel to receive them. Inverting mattress sutures should catch the submucosa but not penetrate the mucosa and should be tied tightly enough to hold serosal surfaces in apposition without strangulating the tissue. Inversion of too much of a diaphragm is to be avoided.
- 8 Accuracy in approximating the edges of the mesentery and in reperi-tonealizing denuded areas
- 9 Isolation of the field of resection and exclusion of contaminated gauze, instruments, towels, and gloves from the field before reperi-tonealization and closure of the wound
- 10 The use of continuous gastric aspiration until obstruction is relieved and for the immediate preoperative and postoperative period
- 11 The provision of adequate hydration and nutrition and the prevention of atelectasis after operation

Although Kennedy⁸ found polyposis rare in children, he believes it is hereditary. McKenney⁹ offered support of inherited tendency by reporting on a woman who had four children by two husbands, all of the children developed the disease. Lockhart-Mummery and Dukes¹ found evidence of a strongly inherited predisposition in all ten of the families in their study, although in one instance all members of one generation escaped both polyposis and cancer. The successive generation, however, had the disease again. Pfeiffer and Patterson¹⁰ found a definite hereditary tendency in five cases. Hardy¹¹ reported a woman 23 years old in whom he believed the disease to be congenital. McKenney⁹ also thought the disease may sometimes exist at birth. He has observed a child 2 years of age with well established polyposis, three older siblings have more advanced stages, each in accordance with age. The two families reported at this time show hereditary instance. In one family the father and three children were afflicted, in the other the father had cancer of the stomach, and the son polyposis of the colon with malignancy in three areas.

McLaughlin¹² in 1943 collected from the literature 331 cases of multiple polyposis of the colon to which he added one case. Since that time there have been reported, in the available publications, two cases by Pugh and Nesselrod,¹³ five cases by Hickman,¹⁴ five cases by Pfeiffer and Patterson,¹⁰ and three by Rachet, Busson, Galmiche, and Rosey.¹⁵ To this group of 347 cases of polyposis of the colon the following five cases are added.

CASE 1—M. H., a 45 year old man, was admitted to the Strong Memorial Hospital, Jan. 11, 1936 because of diarrhea which began five months earlier, rather suddenly, while he was on a vacation. One month later movements became nearly normal and remained so for another two months. At that time diarrhea returned with urgency and, on occasions, partial loss of control. The patient noted that exposure of his back to cold brought on immediate movement. One month before admission he passed, for the first time, 4 or 5 cc of blood. Following this period he had tenesmus and crampy pain in the left lower quadrant. He was constantly tired and listless. One week before, as a result of the first medical treatment, he used boiled skim milk without improvement. He passed blood again at the end of the movement. The day before admission there was marked abdominal distention, severe crampy pain in the left lower quadrant, flatus and an explosive watery movement, ending with 5 cc of blood. He had pyrosis and vomiting on this day also. There were no other symptoms.

Earlier history revealed that he had lost fourteen pounds during the past two years weight at time of admission being 124 pounds. He had always had carious teeth, with repeated apical abscesses. He had passed satisfactory yearly examinations at his shop, however, one year before, hemorrhoids were noted for the first time. He had vague low back pain for six months, attributed to a partial fall in his shop. There were transient paresthesias of all extremities for the preceding week.

He was married. His wife was alive and well. There were five children alive and stated to be well: male 24, female 20, male 18, female 9, and female 4 years of age. His father was alive and well at 81 years, his mother well at 78 years. There were nine siblings, five alive and well, two dead of accidents, one sister with colitis, unexamined, one unknown.

He worked in a dental construction factory, his habits were not remarkable.

Examination revealed a well developed small man with evidence of recent weight loss. Vital signs were normal. The left pupil was .5 mm smaller in diameter than the right. Both reacted to light. A nasal septum deviated to the right, a non tender exostosis of right mandible, complete adentia. There was a soft, blowing, apical systolic murmur without transmission. The abdomen was slightly distended, with mild tenderness over the course of the entire colon, which was easily palpated throughout. Roentgenogram studies of the colon

FAMILIAL POLYPOSIS OF THE COLON

TWO FAMILIES, FIVE CASES

PRIMPTON, GLYTHA, M.D., ROCHESTER, N. Y.

(From the Department of Surgery, The University of Rochester School of Medicine and Dentistry)

FAMILIAL polyposis of the colon

en

pro

... in a high percentage of cases.

It would seem that, unless other evidence than a single case were established in a family such as malignancy of the bowel or stomach, that case cannot be considered in this group.

Menzel in 1721, is credited¹ with being the first to report this condition. Later, in 1861, Luschka² described the condition in a woman 30 years of age. Two years later 1863, Virchow³ gave the first accurate pathologic description. It was however, Cripps⁴ in 1882, who added the important factor of multiple related cases in establishing the authenticity of the disease. He described accurately the clinical manifestations of three cases occurring in a single family.

Since that time there have been extensive studies of several families. Lockhart Mummery and Dukes⁵ have reported ten families with multiple occurrences in each of three or four successive generations. McKenney⁶ has observed three families all in their third generation with this disease—in all twenty-one cases. Friedell and Wakefield⁷ reported a family descended from a brother and sister with polyposis now in the third generation. There are forty-nine members nineteen of whom have either multiple polyposis or cancer of the large bowel. Rankin⁸ reported three families in which polyposis has existed. Falk⁹ reported a family of seven children, six of whom had polyposis, the father had died at 48 years of age from cancer of the rectum. There is very convincing evidence in over 50 per cent of the reports of cases that the predisposition to polyposis is hereditary. The fact that a certain number of cases have apparently occurred singly may be attributed to various factors. Descendants of these isolated cases would according to the law of heredity demonstrated in the earlier families, develop the disease.

The direct factor causing the proliferative tendency in the colonic epithelium is unknown except that it behaves as a mendelian recessive and is transmitted by genes. It would seem, also that this factor is similar to that causing adenocarcinoma of the large bowel, for those individuals in these families who escape polyposis, in a great many instances, develop localized carcinoma of the colon or rectum at an earlier age, by several years, than the average. It is believed that this inherited factor accounts for a large share in the development of polyposis and the precipitating cause if any, a small share.



Fig 2.

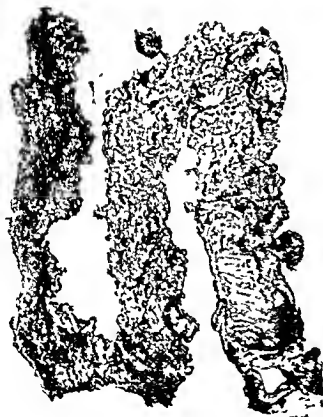


Fig 2.

Fig 2 (Case 2 D H) —Left, roent genograms of colon filled. Only large polyps show as separate dark shadow. Right, partially evacuated colon, note the polyps in proximal sigmoid and the redundancy and dilatation of the same structure.

with barium revealed a dilated and atonic rectum and colon suggesting a long standing obstruction in the lower rectum.

Laboratory examinations were normal except white blood cells, 12,400, neutrophils, 90 per cent, lymphocytes, 6 per cent, monocytes, 4 per cent, and stool contained blood.

There were numerous external hemorrhoids and a tender movable mass lying in the anal canal, several other movable small masses were felt in the lower rectum, and 2 cm. above the inner anal orifice there was, mostly posterior, an indurated mass without a crater, obstructing the lumen by one third, but not adherent to the outside bowel wall.

Proctoscopy revealed a broad based indurated mass, vascular, friable, and un ulcerated. There were many polyps of varying sizes. Biopsy revealed active carcinoma.



Fig. 1 (Case 1 M II) —Roentgenogram of rectum and colon showing dilatation and extensive polyposis throughout. The significance of these shadows was not realized until after sigmoidectomy.

Treatment consisted in

Two weeks after admission a weeks later a right sided col charge of bloody mucoid thin material from both openings, the rectum and sigmoid lumen. Malnutrition increased temperature was mostly 5°C subnormal, and six weeks after hospital admission he died of inanition.

Post mortem revealed extensive polyps through large bowel and carcinomatous degeneration of a broad based lesion extending into the muscular layer of the lower rectum.

CASE 2—D H 21 year old woman the second child of the first patient (Case 1), was first examined June 6 1936 because of intermittent attacks of diarrhea lasting a few days at monthly intervals for two years. Blood in the stool had been observed once, about three months before. Rarely there was burning after movements.

Pro

as a result of polyposis of colon

Hospitalization for colectomy was urged but refused.

She was next seen two months later on Aug. 6, 1936. The first month of the interim history had been unchanged from that before. Then rather suddenly there was continual diarrhea of eight or more stools daily increasing until the past week when she was constantly on the bedpan. Her strength rapidly left her. Intermittent periods of coma had

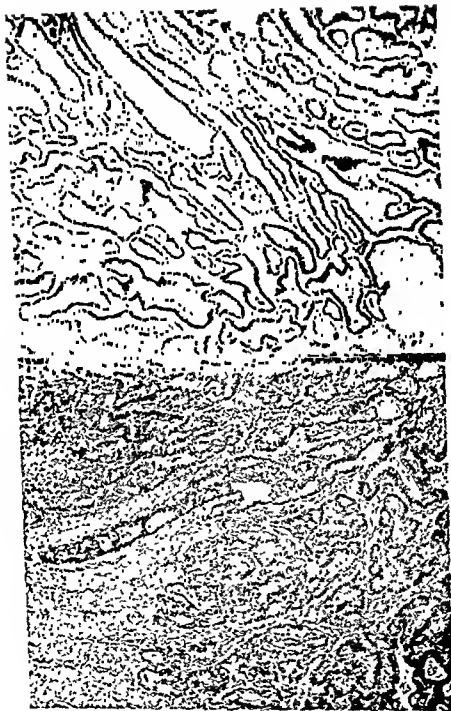


FIG. 4 (Case 2, D II).—Photomicrographs. Top adenomatous polyp ($\times 50$). Bottom, adenocarcinoma invading muscularis of the colon ($\times 100$).

been present for one week there was five pounds loss in weight and for one day before admission nausea and vomiting were frequent

Examination revealed an emaciated and dusky person with apathetic, noticeable weight loss and marked dehydration. Vital signs were normal there was moderate tenderness along transverse and descending colon but no mass was palpable the rectum was filled with soft movable polyps

Laboratory studies were negative except a white blood cell count of 10,000 and hemoglobin of 11.5 Gm per cent. Stool was strongly positive for blood

The patient was given a seven day course of treatment of fluids glucose and whole blood transfusions. Eight days after admission during local anesthesia, an ileostomy was performed. However she continued to have violent diarrhea with watery mucus and blood. She had nausea and repeated vomiting four days postoperatively she became cyanotic and comatose and died thirteen days after admission. Postmortem examination of the colon showed the mucosa to be entirely covered by polyps of all types. Several polyps in each section of the colon measured 6 cm in diameter. There was a hard firm gray white annular ring of tumor tissue 60 cm above the rectum, entirely encircling the lumen and 3 mm wide. 9 cm below this mass there was a large broad based firm polyp. Microscopic section through both of these areas showed adenocarcinoma. There were no enlarged lymph glands or metastases found.

Case 3 - A 19 year old son of the first patient (Case 1) and brother of two others (Cases 2 and 4) was admitted to Brown Memorial Hospital May 3 1936 because of rectal bleeding of three months duration this occurred as spotting on his clothing and had no relation to movements. There were infrequent periods of mild diarrhea. There were no other symptoms

Until a few days before he had admitted he had entirely well.

He was a well developed rather thin boy with no evidence of weight loss who seemed nothing on examination except multiple polyps in the rectum

Laboratory examination showed white blood cell 10,000 hemoglobin 13.7 Gm per cent. Roentgenogram showed polyps throughout the entire large bowel

Proctoscopy revealed the rectum nearly filled by polyps. Biopsy of one revealed mucous glands and cells which had broken through the basement membrane

Treat

At first

four days

performed through a laparotomy

On Feb 18 1937 the abdomen was opened the sigmoid resected on the anterior border many polyps fulgurated and the proximal end of the transected ileum anastomosed

On April 10 1937 a resection of cecum and right colon to the midline was done. The section of bowel was 4 cm long 8 cm in diameter and weighed 900 Gm. There were considerable polyps throughout the large intestine measuring 3 cm in diameter. Two months later

It was
removed
brought

During the next three months the sigmoid was freed of polyps by distal resection on four occasions

At the end of 1937 the sigmoidectomy was closed. During September 1938 volvulus occurred requiring laparotomy

When checked in March 1939 numerous polyps could be demonstrated in the rectum and sigmoid by direct visualization or by barium and roentgen films. However it was not possible to resect the remaining sigmoid and upper rectum was done

The patient was next seen seven months later, May, 1940, he was active and working daily. Weight was 125 pounds, his greatest—and about normal for the family stature. He had three semi-formed stools daily. Examination showed a few rough areas in the rectum which were not considered definite polyps. He was requested to return in three months.

However, he did not return until July, 1941. During the interim there had been a gradual increase in the number of stools up to six daily of a persistent watery type. Fulguration was carried out; biopsy showed no malignancy. One week later it was necessary to tie an internal hemorrhoidal vein. During August, 1941, it was necessary to dilate the low rectum on two occasions as the extensive scarring of the fulgurations had contracted to form an obstructing ring.



Fig. 6 (Case 3, A. H.)—Surgical specimen of cecum and right colon, 34 cm. long, 8 cm. in diameter, weight 900 Gm. A normal specimen of this extent would weigh approximately 200 Gm. This area represents the most active polyposis encountered. The dark area in mid-cecum is a short pedicled polyp.

A biopsy during October, 1941, for the first time showed definite carcinoma. A two-stage abdominal perineal resection was carried out immediately, excising as widely as possible; there was already an indurated mass posterior in the rectum involving the whole thickness of the wall.

Six months later, March, 1942, there was active tumor in the reopened perineal sinus. This was resected. During August 1942, an orchidectomy was done. The patient was last seen one month later and died about the end of the year.

In all, this patient had twenty-eight trips to the operating room, excluding diagnostic proctoscopies and transfusions.

(CASE 4—P. H., 11 year old girl was the fourth child of the first patient (Case 1). She was admitted to the Municipal Hospital, Dec. 14, 1937, with a complaint of loose stools for six months. There was no blood or mucus, or weight loss. Because of the family history and symptoms a barium enema had been taken six weeks before, confirming the diagnosis of diffuse polyposis.

Past history was entirely negative. She was of small stature, undernourished, and pasty in appearance. Vital signs were normal. There was slight distention of the abdomen. Many small soft polyps could be felt in the rectum.

Laboratory studies showed a white blood count of 13,200, hemoglobin, 12 Gm. per cent, negative tuberculin test, otherwise normal.

Between Dec. 16, 1937, and June 2, 1938, four proctoscopic fulgurations were performed, removing adequately all polyps in the distal 10 cm. of the large bowel. In this case the polyps were smaller and more easily visualized than in Case 3.

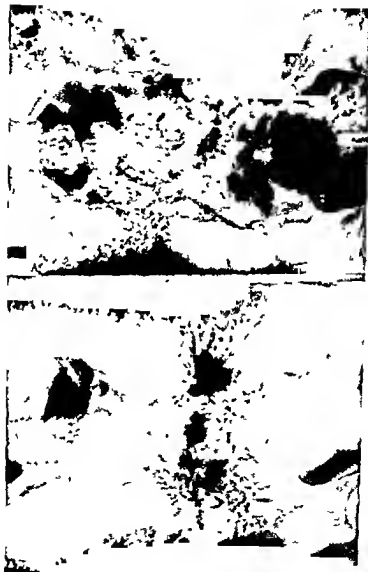


Fig. 6 (Case 7, A, II) — Toxic ulceration. Left, bowel filled with blood. Large polypoid mass in position on lateral border of cecum. Right, ulceration of bowel with an ulceration of polypoid. This was the site of a central polypoid mass.



Fig. 8 (Case 3, A 31).—Photomicrograph of sections of polyps. Top, adenomatous polyp ($\times 60$).
Bottom, adenocarcinoma invading muscularis of the rectum ($\times 100$).

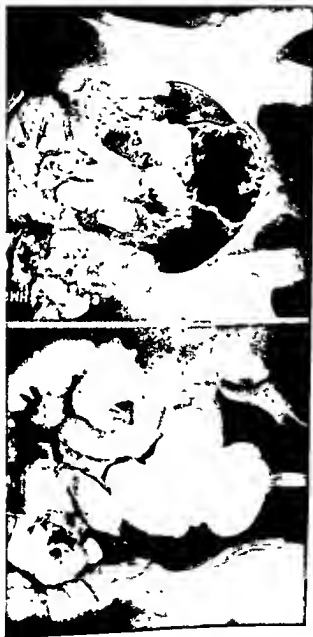


Fig. 7 (Case 3, A. 11).—Icteric specimen taken 19 hr. at the time of the existence of the ileocolic fistula. Left: rectum, lower sigmoid, and many loops of enlarged ileum filled with barium. Right: after evacuation of barium, polyps show as small dark circles. Two are situated over the left sacrocolic junction in the rectum. These are not malignant at this time but subsequently became so in the rectum causing it with four years later.

On June 4, 1938, an appendectomy for acute appendicitis was performed, convalescence was uneventful.

Fulguration of two polyps in the sigmoidal area previously cleared was done on Aug 15, 1938. Two weeks later there were signs of minimal pulmonary tuberculosis and tuberculin skin test became positive. For the three months following, she was observed and treated at the local sanatorium, then released.

On Dec 1, 1938, a laparotomy was performed, the midsigmoid opened, several polyps present were fulgurated, and the proximal end of the transected terminal ileum was implanted, end to side. An ileostomy was left in the mid right lower quadrant.



FIG 11 (Case 4 P II) —Photomicrograph Adenomatous polyp of the colon (X60)

Six weeks later, the cecum and right colon were removed, and after a similar period, the colon and sigmoid were removed down to the anastomosis. Following the discovery of the recurrent polyps in Case 3 at this time, it was decided Sept. 10, 1939, to remove the sigmoid and rectum as low as possible, implanting the ileum into the rectum at the base of the cul de sac. This was done without difficulty, leaving three inches of the rectum.

This girl, although underdeveloped and much underweight, stood all procedures well. During the ten months following the last operation she gained 43 pounds.

Today, seven years later, she is a grown woman of 20 years. She is asymptomatic, weighing 165 pounds, she has one or two movements daily, always well formed. Digital examination of the stump of the rectum shows no polyps. It feels slightly granular on the surface, possibly the scars from fulguration. We will not permit proctoscopy or x ray examination. She is employed by a bank.

CASE 5 —L D is a 39-year old white man, entered the Strong Memorial Hospital, Feb 21, 1941, because of an unexplained anemia. Two days earlier he had consulted his physician about the repair of bilateral uncomplicated inguinal herniae. Examination revealed a hemoglobin of 9.7 Gm. per cent and bilateral herniae. Otherwise all was negative.



Fig 9



Fig 10

Fig 9 (Case 4 P H)—Roentgenograms of colon. Left colon filled with barium. It is enlarged and has typical mottled filling defects throughout. Right, after evacuation, showing polyps in all parts of the colon. All growths are at the same stage of development.

Fig 10 (Case 4 P H)—Roentgenogram of chest showing the intercurrent tuberculous infection which occurred before any abdominal surgery was performed. Patient recovered completely.

Past history also revealed nothing remarkable. His father had died one year earlier of carcinoma of the stomach. Mother and one sister were living and well, one daughter was living and well.

In the hospital the negative findings and anemia were confirmed.

White blood count was 12,200. Stool guaiac was strongly positive. Roentgen studies of the colon were made with difficulty, but showed polyps in the rectum and descending colon and a narrowed irregular, partially obstructed area in the sigmoid, probably carcinoma. Proctoscopy confirmed the presence of many small, sessile polyps in the rectum.

The patient refused a laparotomy which was advised and left the hospital.



FIG 14 (Case 5 L. D.)—Photomicrograph showing malignant degeneration in a polypoid adenocarcinoma of the colon (X40)

He was next seen fourteen months later, April 29 1942, complaining of crampy abdominal pain, weight loss, and blood in the stool, progressive for the past two months. He also noted that for three weeks past bowel movements were more difficult, and the abdomen was increasing in size.

Examination revealed a chronically ill man with marked weight loss. The vital signs were normal. The abdomen was distended tympanic and not tender. A mass could be felt in the left lower quadrant. The rectum had many polyps and an indurated mass about 8 cm. above the sphincter.

A cecostomy was performed, followed two weeks later by an abdominal perineal resection removing 50 cm. of the distal large bowel. A left sided colectomy was formed from proximal segment of the colon.



Fig 1* (Case 3 L.D.)—
Roentgenogram. Barium
enema at time of first ex-
amination showing dilatation
of rectum, obstruction is
complete in sigmoid, and
polyps in entire colon.



Fig 13 (Case 3 L.D.)—
Roentgenogram of colon taken
one year following abdominal
perineal resection of the ter-
minal 30 cm of the large
bowel. Polyps are seen in all
sections of the remaining
colon.

smooth mucous membrane. Malignant areas will appear broad based, invasive of the wall, and diffusely indurated. Occlusion of the lumen results from mass growth or annular invasion. Ulceration of the covering mucosa is uncommon in the degenerated areas.

Microscopically the polyps have a thin core of connective tissue infiltrated with lymphocytes and covered by a markedly hyperplastic columnar epithelium, with many well developed acini. Mitotic figures are numerous. Often also, the cells appear to be infiltrating the supporting membrane.

The acini of the adenoma are equal in size, closely spaced, and lined by a single layer of cells.

The constituent cells of an adenoma which is progressing toward cancer will show colloid degeneration, irregular and uneven growth, and invasion of the basal membrane. Later the cells form abortive acinar structures and cellular sheaths which extend into the submucosal layer of the bowel. Definite adenocarcinoma progressed from this stage.

Malignant degeneration is an intrinsic characteristic of polyposis of the bowel. This fact is attested by the many reports. Hullsiek¹⁶ found 36 per cent of the patients in a collected 127 cases had cancer. McKenney⁴ found in each of three families an incident of 33 per cent of malignant degeneration. Hedin¹⁷ stressed the frequency of intercurrent cancer from polypoid disease. Jones¹⁸ reported a patient who, five years after fulguration, developed cancer of the rectum and died. Miller and Sweet¹⁹ reported a brother and sister both of whom had polyposis and cancer of the terminal large bowel. Pugh and Nesselrod²⁰ believed 100 per cent eventually become malignant.

Four of the five patients reported upon here had malignant degeneration, two of them multiple. However, the death of only one (Case 3) was due to cancer. The other two deaths (Cases 1 and 2) were due to the excessive demand made by the cellular growth on the general body metabolism resulting in fatal malnutrition.

Malignant degeneration occurred in 80 per cent of these five cases, and in 40 per cent it was multiple. In three instances the cancer was in the rectum, twice in the sigmoid, once each in the descending and left transverse colon. Although there is a very marked tendency for local invasion of adjacent tissue, illustrated by the repeated recurrence in Case 3, there appear to be only very late, if any, general metastases. No tumor was found in any of the five cases other than the direct extension into the bladder and perirectal tissue in Case 3. Although polyps occur about evenly in all parts of the large bowel, cancer occurs largely in the terminal 50 cm. Smedal²¹ believed this to result from the trauma of feces.

It would also appear that the cells of the recurrent growths have already taken on an intrinsic change by the time they become macroscopic, for these polyps while still small all are broad based, bumpy in shape, and less friable than the earlier sessile polyps. This suggests that the cells causing these later growths were either already intramural at the time of fulguration of the original polyp, or, if coming from a new area of epithelium, they had developed a

The removed rectum and sigmoid showed many polyps, there were three areas of malignant growth, one in the rectum, one in the descending colon, and an annular lesion measuring 4 cm in diameter in the sigmoid causing the obstruction.

The patient was not seen again. However, it is reported that one year later, March, 1943, he had regained 60 pounds in weight and was carrying on his previous occupation. Roentgenograms showed polyps throughout the remaining colon. The descending colon when viewed through a proctoscope showed many polyps, one 1.5 cm. in diameter was described as appearing malignant. Over this region he received 500 R of x ray therapy.

He is now living in the West, carrying on a business. He apparently has no symptoms.*

Of this family of seven people, apparently all well as late as the summer of 1935, three remain who do not have evidence of the disease. The mother at 55 years and the youngest daughter at 15 years are both asymptomatic and apparently well. They refuse examination. The oldest son at 34 years is known to be free by early roentgenograms and a proctoscopy during the past three months.

The second family has but one case of true polypoid disease. However, this is typical in its manifestations, being present in a diffuse form in all parts of the large bowel, as irregular, mucus covered multiformed polyps. The patient also had the typical malignant degeneration in three places in the left sided large bowel. There was one patient with carcinoma of the gastrointestinal tract.

It is believed that other cases could be discovered in this family if examination were permitted. The fact that the existence of relatives can be established by Social Service and that they are apparently asymptomatic does not exclude polypoid disease.

The diagnosis of polyposis is made from the history, digital examination of the rectum, proctoscopy, and roentgenogram of the colon. Of these the contrast barium and air replacement enema is the most important. Only this can show the diffuse polyps in all sections of the bowel with the characteristic mottled effect from barium on the surface and in the interstices of the polyps.

The surgical specimens of the colon or rectum are essentially the same in all cases excluding the added pathology resulting from a superimposed carcinoma. The bowel is uniformly larger than normal, the haustral markings persist, the serosal surface in appearance is normal. The adjacent mesentery is often thickened and edematous, with several soft enlarged lymph glands. The colon when palpated is heavy, does not collapse on pressure, and feels rather soft. Areas of malignancy can be determined by constriction, scarring, or induration which is in marked contrast to the rest of the bowel. The weight of the bowel is greatly increased. The entire large bowel to the midsigmoid of one patient (Case 3) weighed 1,825 Gm, whereas that corresponding from a normal adult would be 440 Gm. When opened the mucosal surface is mucus covered and glistening in appearance. It is everywhere closely placed villous and sessile processes which, when large, the tissue is soft and friable.

*Since this report was submitted, this man has returned with an extensive neoplastic process involving the left colectomy and abdominal wall. Complete colectomy has been successfully performed.

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tendency toward degeneration before becoming a visible mass. The latter hypothesis is more acceptable for the destruction of all existing polyps does not in my belief eradicate the intrinsic urge of the epithelium to proliferate.

Treatment by x ray over the entire colon is the only conservative therapy available. This would seem illogical from the beginning because the well-differentiated cells of the adenoma should be radiation resistant. One patient (Case 3) received one year after extensive abdominal perineal resection two courses of 800 r each of x ray therapy over the remaining colon with apparently some benefit. However it is well to bear in mind the fact that this patient had had the terminal 30 cm of the bowel removed which was the cancer area.

The available reports are not enthusiastic. Vanzant⁹ treated two patients with x ray for one and one half years with benefit but does not feel that such management is ideal. In a personal communication McKennan has observed the progress of tumor growths following heavy radiation in individuals refusing surgery.

The removal of polyps through multiple colostomies was used by Hedim¹ and recommended in selected cases. However, to me it would seem a physical impossibility to destroy adequately the polyps as they occur in a true case of familial polyposis. Even if such were accomplished once the colostomies were closed the surgeon would lose all chance of subsequent inspection of the mucosa which is essential in permanent cure. The use of the colonoscope as suggested by Hedim¹ would appear helpful but at best inspection can be carried out only to the splenic flexure of the colon. Other means for treating the disease present in the transverse and right colon would have to be added.

Rankin² in 1930 advocated total colectomy but later³ 1937 modified this to a temporary ileostomy with subsequent colectomy and ileosigmoidostomy. Miller and Sweet¹⁰ treated two patients by complete colectomy. Jones⁸ reported a patient treated by ileosigmoidostomy, colectomy and fulguration of remaining bowel. However this patient died four years later from recurrence in the pelvis. McLaughlin⁷ found in 1943 thirty nine patients treated by surgery as shown in Table I. The cases added are those of McLaughlin¹² 1, Pugh and Vesselrod¹³ 2, Hickman¹⁴ 3, Pfeiffer and Patterson¹⁵ 4, the author 5.

TABLE I

	1941	NEW CASES	TOTAL
Ileostomy and total colectomy	1	1	1
Ileosigmoidostomy colectomy	13	13	6
Partial colectomy	3	0	3
Ileostomy	1	0	1
Ileosigmoidostomy			
Abdominal perineal resection		1	1
Anastomosis ileum to low resection		0	0
Total			38

It will be noted that during the past four years especially there has been a predominant choice of ileosigmoidostomy with fulguration of the remaining large bowel from below or through a temporary external sigmoidostomy. Lockhart Mummery¹⁶ advocated this method and used it in several instances. The

two patients whom I reported as having the ileum anastomosed to the rectum earlier had ileosigmoidostomy. However, recurrence of polyps in the sigmoid in one (Case 3) necessitated resection of that stump and part of the rectum. In another (Case 4) this procedure was carried out as an elective, to eliminate all polyp bearing mucosa and still preserve the sphincter.



FIG 1.—Diagram illustrating type of operation recommended

At the time of this resection a change in the terminal ileum was noted. The diameter was increased by 50 per cent, the serosa was grayish and granular, and the wall was firmer than usual. Whether this is a localized ileitis as suggested by Hickman¹⁴ or a change incident to the altered physiologic function of the small bowel can be determined only on more observations. It is apparent, however, that the small bowel assumes certain new function, since both of these patients with no more than 8 cm. of rectum had essentially normal stools twice daily.

It is my opinion that all polyp bearing mucosa must be removed and any segment of the rectum left with the sphincter should be sufficiently short to be as fulgurant at all times. And even this may be done with wisdom only when the

THE EFFECT OF STREPTOMYCIN IN "CLOSED LOOP" APPENDICITIS

AN EXPERIMENTAL STUDY

JACK M. FARRIS, M.D., LOS ANGELES, CALIF., AND
HOWARD H. ROMACK, M.D. (BY INVITATION), CAMBRIDGE, N. Y.

CHEMOTHERAPY as an adjunct in the treatment of peritonitis of appendiceal origin occupies an important role in the armamentarium of the modern surgeon. The sulfonamide drugs have been credited with significantly lowering the mortality rate in spreading peritonitis as a sequel to appendicitis¹. More recently penicillin has received attention in this connection².

The purpose in conducting this experimental study was to investigate the effect of streptomycin upon the course of obstructive "closed loop" appendicitis in experimental animals. Because of its selective action upon the gram negative intestinal flora it seemed that this drug likewise would be a significant factor in combating peritonitis of intestinal origin.

The bacteriologic aspects of appendiceal peritonitis in man emphasize the important role of the gram negative colon bacillus. Appendiceal exudates in man contain *Bacillus coli* in 85 per cent of the instances, and in over 60 per cent of the cases the gram negative colon group is predominant³. The intestinal streptococci, in general, are considered nonpathogenic except for their reinforcing effects upon sublethal doses of *B. coli*. These facts suggest that a drug acting primarily upon the gram negative organisms (streptomycin) would offer advantages in the treatment of appendiceal peritonitis over drugs which act primarily upon the gram positive organisms (sulfonamides and penicillin).

EXPERIMENTAL METHODS

Thirty young adult rabbits, weighing between 2 and 3 kilograms, were used in this study.

Controls—Ten animals served as controls. Intravenous nembutal was the anesthetic agent. The abdominal area was carefully prepared with 5 per cent tincture of iodine and 70 per cent alcohol and suitably draped with sterile linen. All instruments were sterilized by boiling. A three inch transverse subcostal incision was made on the right and the appendix identified. In one group of animals the blood supply to the appendix was completely sacrificed, the appendix crushed at its junction with the cecum, and ligated with a heavy silk suture. In the other group crushing and ligation were carried out with the meso-appendix intact. In a few animals saline washings of the appendix were obtained through a hypodermic needle for bacteriologic study. In all animals the appendix was distended by the injection of a sterile radiopaque medium (lipio-

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This study was carried out while the authors were associated with the Department of Surgery, University Hospital, Ann Arbor, Mich.

dol or 70 per cent diodrast) The small needle hole through which the radio-paque substance was injected was reinforced with a mattress suture of fine silk. The appendix was then replaced into the abdominal cavity and the wound closed. Serial x ray views were taken. Food and water were provided. No parenteral supportive therapy or chemotherapy was used. The procedure was carried out with a minimum of trauma and blood loss so as to provide standard conditions.

Local Streptomycin—Ten animals served for an identical experiment except for a single local injection of streptomycin into the lumen of the appendix at the time of operation. The blood supply to the appendix was sacrificed in all of the experiments. After the appendix was devascularized and ligated at its base, a single dose of streptomycin was injected into the lumen of the appendix. The streptomycin was dissolved in sterile distilled water, 1 c.c. contained 50 000 units. Three animals received a single 25 000 unit dose of streptomycin. Four animals received a single 50 000 unit dose. Three animals received a single 100 000 unit dose. No further treatment of any kind was given.

Systemic Streptomycin—Ten animals served for an identical experiment except that streptomycin was given parenterally rather than locally. In five animals treatment was begun at the conclusion of the operation. In five animals six hours elapsed before parenteral treatment was begun. Treatment consisted of an intramuscular injection (25 000 units) every six hours. Treatment was continued for a total of sixteen doses so that each animal received 400 000 units of the drug. Streptomycin was not put into the lumen of the appendix as in the previous group.

RESULTS

Controls—Nine of the control rabbits were dead in less than forty hours. Four of the animals in the group of ten succumbed between the eleventh and twentieth hour, three died between the twenty first and thirtieth hour, one died between the thirty first and fortieth hour, the ninth died between the forty first and the fiftieth hour and one animal survived. Autopsies uniformly disclosed a diffuse peritonitis. The appendix ruptured in every instance followed by a fulminating severe lethal peritonitis. The sequence of events following ligation of the appendix is illustrated in the serial roentgenograms in Fig 1. The lipiodol filled appendix in these two animals ruptured before the twentieth hour with dissemination of the contents into the free peritoneal cavity. Both of these animals were dead before the thirtieth hour.

The symptomatology was identical in all animals. They developed profound prostration soon followed by abdominal distention and rigidity. The autopsy findings were practically identical in all animals. There was always a point of perforation in the appendix. If the blood supply was left intact the area of perforation appeared to be somewhat smaller than in the devascularized group. In no instance did perforation occur at the site of ligation of the base but rather in the body of the appendix. There was usually a small amount of foul smelling bloody fluid in the peritoneal cavity. This procedure produced a pathologic lesion identical with so-called closed loop intestinal obstruction.

1.



2.



3.



4.



1.



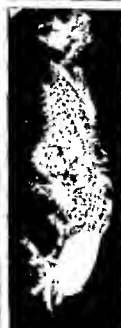
2.



3.



4.



The appendix in the rabbit is relatively larger than in man (Fig 2) When obstructed, it rapidly becomes distended and uniformly perforates, thereby seeding the peritoneal cavity with a large inoculum of pathogenic organisms. The resulting peritonitis with its attendant symptomatology and pathologic changes is similar to that observed in man.



Fig 2—Illustration of the appendix of the rabbit with a ligature at the base. When thus obstructed an isolated intestinal loop is provided for experimental observations.

Local Streptomycin—All ten animals in this group survived as a result of a single intraluminal injection of streptomycin. The postoperative course in this group of animals was indeed striking when compared with the controls. The animals at no time appeared sick and all took food and water freely within twenty four hours. They all gained weight and showed no ill effects from the operative procedure. They were all sacrificed at intervals of one to four weeks and autopsies performed.

Autopsy findings were identical in all instances. There was no evidence of peritonitis. It was difficult to obtain enough peritoneal fluid to moisten a cotton applicator for bacteriologic study. There were no adhesions between the peritoneal surfaces. The appendix had not ruptured in any of the animals. In every instance it appeared to be distended to about five times normal diameter which

debris and inspissated fecal material. The wall of this cavity when studied microscopically bore no resemblance to the normal histologic appearance of the appendix. In effect, an "autoappendectomy" had occurred. In every instance the peritoneal cultures were negative. The cultures from the cavity showed no pathogenic organisms, but in a few instances a few of the organisms of the "soil and water" group were grown. It seemed apparent that sterilization of the lumen of the appendix had occurred, and even in the presence of total gangrene of the appendix the animal had received complete protection from peritonitis. Fig 3 illustrates the roentgenograms on two different animals in this group. These views, taken twenty one days after operation, indicate that the appendix still contains the lipiodol and the wall is intact. This suggests that mechanical factors alone are not sufficient to produce rupture in an obstructed gangrenous appendix.



Fig 3—A Rabbit 25th twenty one days following ligature of the appendix. B Rabbit 106 twenty one days following ligature of the appendix. (Note the intact appendix as evidenced by contained lipiodol.)

Systemic Streptomycin—Nine of the ten animals used in this experiment survived. There was no significant difference in the group receiving immediate parenteral streptomycin and in the group in which six hours were allowed to elapse before such treatment was instituted. The single animal that died had received 25,000 units of streptomycin intramuscularly immediately following operation. Death occurred twenty four hours after operation, and a total of 175,000 units of the drug had been given. Autopsy showed a large hematoma in the mesentery of the small bowel. The appendix had not perforated and

there were no signs of peritonitis. It was felt that this was an operative death concomitant with faulty technique.

The remaining nine animals survived and were autopsied at intervals of one to ten weeks. One of the animals that was sacrificed four weeks after operation showed signs of a peritonitis inasmuch as there were multiple fibrinous adhesions between all loops of intestine. However, this animal had appeared perfectly healthy and had gained weight throughout the experiment. The other animals were remarkably free of adhesions and the peritoneal surfaces appeared entirely normal. The appearance of the appendix was strikingly similar to that observed in the group treated with local streptomycin. An "autoappendectomy" had occurred. A cavity remained with a well-developed wall containing a small amount of odorless, yellowish, cheesy material which on culture did not show the presence of pathogenic organisms. There was never any free fluid in the peritoneal cavity. Autopsy performed on one animal ten weeks after operation showed the remains of the appendical appendage to be less than 1 cm. in diameter and length. Histologic examination of the appendical remains showed nothing but a granulation wall without the cellular characteristics of the normal appendix.

It was our general impression, however, that these animals had an immediate postoperative course less smooth than that observed in the group treated with local streptomycin. It was generally somewhat longer before they began to take their food and water with relish. In the animals sacrificed at one week there were definite signs of local peritonitis. The appendix was covered with a heavy layer of fibrinous exudate, although it had not ruptured. It seemed apparent that all of these animals developed a low grade peritonitis which subsided under parenteral streptomycin therapy.

COMMENT

Rabbits were chosen for this experiment because of their availability. A theoretical objection to the use of rabbits rather than dogs might exist because of the absence of the anaerobic flora, notably *Clostridium welchii* in the intestinal tract of the former. However, the significance of these anaerobes has remained an uncertain quantity, as to both incidence and etiologic significance. An exhaustive review of the subject has been reported by Bower and associates.⁴ It is practically undeniable that among the aerobic microbes the primary role is played by the *B. coli*. It is also rather generally agreed that *Cl. welchii* is not particularly virulent in the peritoneal cavity and that it is essentially saprophytic rather than pathogenic.⁵ For these reasons we felt that rabbits would serve satisfactorily.

The contrast in the results obtained in the animals treated with streptomycin when compared with the controls needs little comment. It is apparent that this drug is a potent agent against the bacterial flora of the intestinal tract of the rabbit (primarily *B. coli*). The failure of the blind appendical loops to rupture in the treated group lends support to the view that the bacteriologic aspects of closed loop intestinal obstruction are of greater significance than other allied theories relative to the concomitant "toxemia." The failure of the appendix to rupture after ligation and devascularization in the treated group

FEMORAL HERNIA WITH GANGRENOUS BOWEL

CLARENCE DENNIS, M D , AND RICHARD L. VARCO, M D , MINNEAPOLIS, MINN.

(From the Departments of Surgery, University of Minnesota Hospitals and
Minneapolis General Hospital)

FEMORAL hernias are attended by strangulation in a far greater proportion of the cases than is true in inguinal or ventral hernias, the figure being as high as 32 per cent in one series.¹

In speaking of hernia, certain terms must be precisely used to clarify the subject under discussion. "Strangulated hernia" is defined by Dorland as "one which is tightly constricted and has become or is likely to become" gangrenous. In the present paper we are concerned with hernias in which contained small bowel has actually become partially or wholly gangrenous.

In such cases with dead intestine in the sac, the published mortality rates are very high. Jens lost eight out of twelve patients and a rather extensive review of the literature by Gatch and Montgomery uncovered only one report of five or more cases with a mortality as low as 20 per cent.

The reasons for the formidable risk of such situations seem to us to fall under four main headings:

- 1 Local or peritoneal infection
- 2 Systemic and pulmonary complications due to the intestinal obstruction
- 3 Fear of section of the inguinal ligament and
- 4 Fear of primary anastomosis

CONSIDERATIONS IN THE SURGICAL MANAGEMENT OF FEMORAL HERNIA WITH GANGRENOUS BOWEL

The conventional method of caring for patients with femoral hernia with gangrenous bowel consists in exposing and opening the hernial sac at the outset, enlargement of the neck is necessary to permit delivery of more bowel and either exteriorization or resection of the contaminated field. The method of Gatch and Montgomery.

The risks of resection and primary anastomosis by older methods have been too high to justify the use of those methods. In most instances in which such cases have been reported the field has been initially contaminated by opening the sac and further soiled by performance of an open anastomosis. Disaster has further been courted by use of absorbable suture material for the anastomotic procedure.

Certain alternative methods have been presented. Mulvaney employed a temporary single barrel ileostomy and multiple procedures to avoid the need for anastomosis in the presence of obstruction and gangrene. Gatch and Mont-

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gomery were successful in three cases in which the incarcerated bowel was incised to make the external fistula decompression of the previously obstructed gut was aided by use of the Miller Abbott tube, and resection of the incarcerated ileum and anastomosis of the remaining ends were accomplished as a final procedure

MINNESOTA METHOD

We have devised a method of caring for these cases which we believe to be superior to any of those previously proposed both as to immediate safety of the patient and as to saving of hospital bed days for him

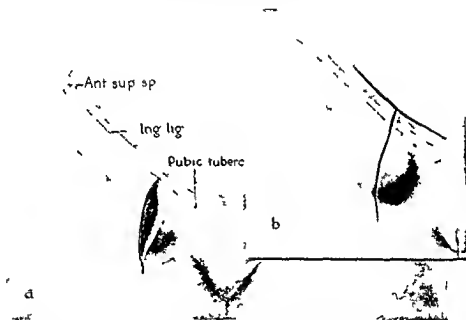


Fig 1—Skin incision a For recognition of gangrene without opening sac b completion of incision after recognition of gangrene

The stomach is emptied with a Wangenstein tube and suction apparatus and the patient is supplied with water and salt as needed. We usually find that he does well on 7 per cent of his body weight intravenously in the first twenty four hours one half of this is 0.9 per cent NaCl and one half as 5 per cent glucose in distilled water. Ordinarily one third to one half of this is given in the three hours employed in preparation for surgery. The patient is weighed and hemoglobin hematocrit blood urea nitrogen chloride and serum protein levels and carbon dioxide combining power are determined as further guides to fluid therapy. A catheter is placed in the bladder.

Under local block anesthesia a vertical incision is made over the bulge in the groin and carried cautiously down to the peritoneal sac. The contents of the sac can be visualized through the remaining wall bloody fluid pus feces or blue bowel can usually be readily recognized (Fig 1 a)

In case any of these indicates the presence of gangrenous bowel, dissection in this area is discontinued, and an incision is made 2 cm. above the inguinal ligament and parallel to it, and the vertical incision is continued upward to it to make a T shaped incision (Fig 1, b). The aponeurosis of the external oblique muscle is split parallel to the ligament and about 1 cm. above it and extended into the external inguinal ring. The margins of the internal oblique and transversus muscles (and the cord if the patient is a male) are elevated, the deep epigastric vessels are divided and ligated, and the peritoneum is incised parallel with the oblique skin incision (Fig 2).

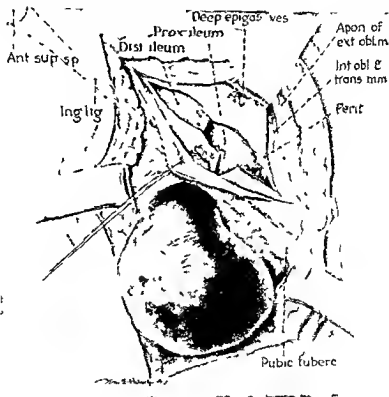


Fig 2—Incision in peritoneum for exposure of structures entering sac.

From this vantage point, the viscera entering the hernia may be easily seen. Omentum if involved, is easily divided and ligated close to the neck. The small bowel entering the sac is prepared by division of the mesenteric attachment from the proximal to the distal side of the incarcerated loop of bowel. Two Ochsner clamps are placed across each of these limbs of bowel, and the ileum is severed between each pair with the cautery.

The gangrenous sac contents having been freed from intra abdominal attachments, the inguinal ligament is divided close to the pubic attachment and split laterally, leaving enough heavy aponeurotic tissue applied to the front

of the neck of the sack to prevent relaxation of the neck and release of the soiled content. The sac is encased in a rather firm layer of fascia derived from the femoral canal. Dissection outside it frees the entire sac except for the residual fibrous portions of the ring which can then be cut under direct vision from the surrounding tissues and left on the neck of the sac (Fig 3). Palpation for an anomalous obturator artery adds an item of safety here.

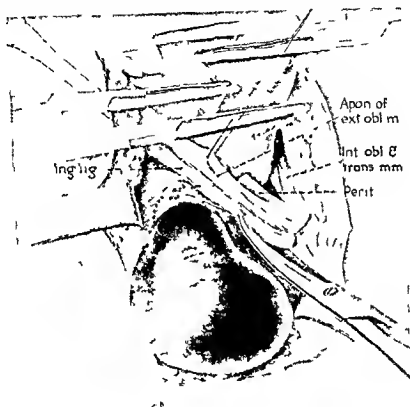


Fig 3—Separation of neck of sac with retention of intact fibrous ring

The entire contaminated area may then be removed intact without soiling of the remaining field (Fig 4).

Further preparation of the remaining bowel ends may then be done easily, and oblique aseptic end to end anastomosis is performed as for any case of resection in the presence of obstruction. Following closure of the mesentery the bowel is dropped back into the abdomen. Performance of the anastomosis is facilitated by placement of the posterior silk row as interrupted Cushing stitches before use of the running crutch.

Closure of the peritoneal defect in the repair of the hernia is easily accomplished because of the usual mobility of the peritoneum in this area. Closure is usually made by interrupted mattress sutures of 2-pound test silk, approximating the margins of the defect resulting from excision of the sac.

in a vertical line (Fig 5) and closing the original oblique peritoneal incision in a line parallel with the original opening (Fig 6)

Repair of the hernial and surgical defect is simplified by application of the principles of the McVay Harkins modification of the Lotheisen hernio-

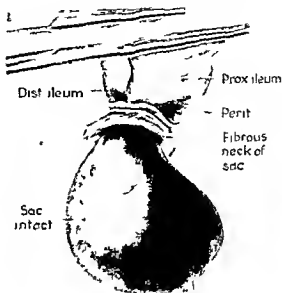


Fig 4—Sac removed

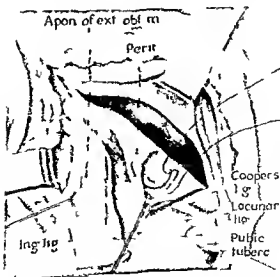


Fig 5—Closure of peritoneal defect within abdomen.

plasty The margins of the internal oblique and transverse muscles are sutured to Cooper's ligament as far laterally as the femoral vein (Fig 7) and to the inguinal ligament lateral to that point (the cord in the male ordinarily being left external to this layer) A McVay Harkins relaxing incision may be made in the posterior layer of the anterior rectus sheath if needed to gain approximation without tension

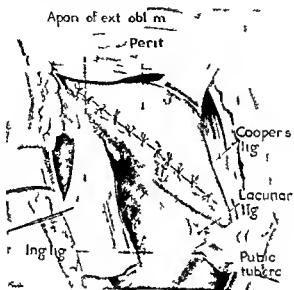


Fig 6—Peritoneal closure completed

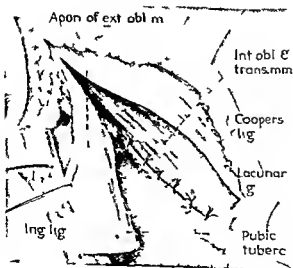


Fig 7—Abdominal wall closure approximation of muscle layer to Cooper's ligament.

The inguinal ligament is restored easily by interrupted sutures of 3-pound test silk approximating it as far medially as it will go without undue tension, to the lacunar ligament and to Cooper's ligament (Fig 8)

The aponeurosis of the external oblique muscle is finally approximated with interrupted silk (over the cord in the male) completing the hernial repair proper (Fig 9) Silk closure of the skin is used without drainage

If no evidence of necrosis is apparent upon first exposure of the sac it is well to dissect the sac rather widely and to place moist packs about it before

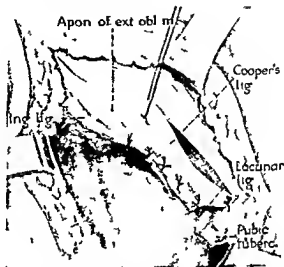


Fig 8—Abdominal wall closure reconstruction of inguinal ligament.

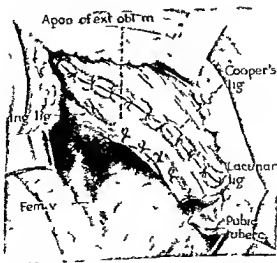


Fig 9—Abdominal wall closure closure of aponeurosis of external oblique muscle.

incision of the sac wall. In one case clean omentum overlay gangrenous bowel and dirty fluid in the sac. The employment of this preliminary dissection permitted closure of the opening in the sac so that the operation could be completed essentially as described.

In case no nonviable bowel is encountered the sac, of course, may be widely opened, the hernia reduced by enlarging the neck medially, and the repair done entirely from below.

RATIONALE OF THE OPERATION

Preparation—Our experience at the University of Minnesota Hospitals has indicated that the severely dehydrated patient has not the stamina to endure even the most careful surgery and that even though the passage of three or four hours might increase the likelihood of frank gangrene in the strangulated bowel, it is a safer course in the long run to spend this time in performance of the blood chemical and hematologic determinations indicated and in appropriate partial hydration at least.

Use of nasal gastric suction need hardly be discussed except to condemn preoperative use of the Miller Abbott tube as dangerously time consuming in such cases. Use of the urethral catheter is an aid to estimation by beginning urine flow of a state of hydration sufficient to allow operation and is a wise precautionary measure to keep the bladder out of the surgical field.

Anesthesia—In our earlier cases general anesthesia was used, later spinal injection was used, and finally we have agreed as Watson does that a good local block offers by all considerations the best relaxation and the safest type of anesthesia. An effort is made to block the ilio inguinal nerve medial to the anterior superior spine of the ilium, the plexus surrounding the femoral vessels, and the intercostal nerves up to the tenth dorsal nerve as they cross the anterior axillary line. Infiltration of the mesentery is essential. Our patients are then awake and do not lose cough reflexes or aspirate regurgitated gastrointestinal content with the facility of the sleeping patient.

Above all dependence on local block anesthesia with reinforcement periodically permits the surgeon to work without the press of urgency so often inherent in the spinal or general anesthetic. We make no apology for expenditure of 2½ or 3 hours for the block and procedure. Restlessness is overcome by settling the patient in a comfortable position in the first place, and by the judicious use of small doses of morphine or pentothal intravenously.

Recognition of Gangrene Without Contamination—Use of a vertical incision over the bulge of the hernia usually permits one to recognize by sight and smell the presence of frank gangrene without opening of the sac. There are some early cases as indicated in Table II in which the sac was incised after such inspection only to find that gangrene had actually occurred. In these instances in which necrosis is not apparent through the intact sac, it is evidently of too short duration to have resulted in either frank pus formation or heavy bacterial contamination, for neither of these was noted in any of these incised cases and healing was uneventful. In those in which gangrene

TABLE I FEMORAL HERNIAS WITH GANGRENOUS BOWEL—RESECTION OF BOWEL AND SAC INTACT

CHART NO	PATIENT	AGE (YR)	DURATION	COMPLICATION	DAYS ON SERV ICE	RESULT
718626	E G	68	36 hr	Suppl infection	21	Well
740093	I A	81	40 hr	Phlebitis (opposite side)	29	Died*
741007	I D	81	2 weeks		14	Well
747475	J M	67	3 days		11	Well
275 47	J W	64	7 days		7	Well

*Died of ruptured aortic arch aneurysm abdomen clean

was apparent through the intact sac, the pathologist usually found either perforation of the bowel or obvious heavy contamination. When gangrene has been found after opening the sac, we have tried to close the sac by packs or forceps, although in two cases this has not been possible.

Importance of Avoiding Contamination—Bacterial contamination of the peritoneal cavity is probably better tolerated than it has been considered to be, even in the absence of our present chemotherapeutic agents. Nevertheless a refinement which obviates this risk is an added measure of safety.

Contamination of the serosal surfaces employed for the anastomosis is probably of much greater importance as indicated in an earlier paper.¹ Use of the present method and of the oblique, aseptic, end to end anastomosis described in that paper seems to answer this requirement.

We consider avoidance of contamination of the tissues to be used for hernia repair the primary aim in resection of the entire sac and content intact. An infected hernioplasty is extremely likely to be a failure.

Avoidance of Absorption of Toxic Products in the Sac and Gut—Knight reported experiments in animals in which release of strangulation obstruction of twenty four hours' duration had led to mild to lethal blood pressure drops depending on the severity of the experimental strangulation. This same argument should apply to man, as indicated by Knight's observation that abdominal fluid and venous blood from clinical strangulation obstruction cases contained depressor substances demonstrable on intravenous injection into cats, this effect was absent in the absence of strangulation, in hydrocele fluid, and in fluid from old hematomas.

TABLE II FEMORAL HERNIAS WITH GANGRENOUS BOWEL—RESECTION OF BOWEL AND SAC INTACT EXCEPT FOR OPENING PACKED-OFF SAC BECAUSE OF DOUBT OF GANGRENE

CHART NO	PATIENT	AGE (YR.)	DURATION	COMPLICATION	DAYS ON SERV ICE	RESULT
721976	F S	50	18 hr		10	Well
2508-45	O R	63	12 hr		17	Well*
2905-45	C B	73	4 days	Heart failure pneumonia	2	Died†
4900 46	J H	62	7 hr	Orthopnea failure	9	Well
327-47	M H	62	48 hr		13	Well

*Content slipped through ring accidentally

†Umbilical hernia, heart failure on admission

Because of these experimental observations it is important to resect the gangrenous segment of intestine without releasing the neck of the sack. A possible result of such substances in the sac fluid is suggested in a recent case of inguinal hernia with strangulation of seven hours' duration and gangrenous gut operated upon by Wangensteen in which this fluid escaped into the peritoneal cavity the patient suffered an extreme degree of ileus which responded to intubation only after several days.

Section of the Inguinal Ligament—Section of the inguinal ligament is regarded by most surgeons (Watson) as an unwarranted step to be avoided at almost any cost. The success in our hands of the McVay Harkins hernioplasty has given us confidence in approximation of the margins of the internal oblique and transverse abdominal muscles to Cooper's ligament as far laterally as the femoral vein. The relaxing incision of the posterior layer of the anterior rectus sheath has been used in some of the cases but has usually not been needed to obtain approximation without tension. Repair of the inguinal ligament by suture of the medial end to the lacunar ligament and to Cooper's ligament seems to have given satisfactory results.

Our follow up unfortunately has been very poor. One patient with an umbilical hernia died within two days. The other death came twenty nine days after a femoral repair as described. In this case the repair was sound at autopsy. Of three patients upon whom follow up studies have been carried out two were without recurrence of hernia at two months and at one year respectively but one developed a recurrence as a direct inguinal hernia two years after repair. We did a follow up on one patient who had section of the inguinal ligament for excision of an arteriovenous fistula for eighteen months he had no sign of weakness here. Another patient had bilateral inguinal dissection for carcinomatous nodes with division of both inguinal ligaments here also observation ten months and three months later showed no weakness. One patient had the entire left lower quadrant resected for recurrent sigmoid carcinoma including the inguinal ligament and leaving only Camper's fascia and the skin here also no sign of weakness was found on straining one year later. In four hemipelvectomies performed by another surgeon* no evidence of weakness in this area resulted. We believe that precise closure of good tissues is much more important than preservation of the initial integrity of the inguinal ligament.

We are perhaps a little conservative but have not allowed these patients out of bed the same day as surgery as we do other groin hernia repairs but have usually kept them down for three or four days that is until after strength gain has begun to develop.

Type of Anastomosis—The considerations favoring use of the closed aseptic anastomosis employed routinely in these cases have been fully discussed in the paper describing that procedure. At the time of submission of that paper sixteen anastomoses had been made in the presence of obstruction fourteen of them with gangrene with two deaths. The record today with about three times that number of cases shows a lower mortality as experience has increased and increasing confidence in the method has been gained. There have

*Dr. John R. Falne

been no further suture line leaks. We have abandoned the local use of sulfonamides as of no proved aid to safety. Although single layer silk anastomoses as proposed by Wangenstein have been generally adopted for gastric and colic anastomosis and for end-to-end ileocolostomies the importance of precision in suture placement in iliac end-to-end anastomosis in obstruction cases where the disparity in diameter of the lumen may be one to two or one to three has led us to continue with the two layer anastomosis essentially as first described.

General chemotherapy with sulfonamides or penicillin has usually been employed, but not in all cases. It seems to us to add as much to the confidence of the surgeon as to the safety of the patient.

RESULTS

Since March 19 1942 ten patients have been treated by the technique described, nine for femoral and one for umbilical hernia with gangrene in each case. Six have been treated at the University of Minnesota Hospitals and four at the Minneapolis General Hospital.*

In five cases (Table I) the procedure was performed just as indicated keeping the sac intact throughout. Of these five cases one patient died. He was an 81 year old man whose strangulation occurred forty hours before surgery and whose wound healed primarily. Ten days after surgery he developed thrombophlebitis on the opposite side which responded nicely to lumbar sympathetic novocain blocks. He died suddenly twenty nine days after operation while dressed and ready to go home. Autopsy showed the wound cleanly healed and the anastomosis in good order. Death was due to rupture of an aneurysm of the aortic arch.

In the remaining five cases (Table II) the sac was opened in three because visualization through the intact sac failed to demonstrate the early gangrene present. In one instance the house officer doing the case before one of the authors was called *did not know of this procedure* (No 327-47) the sac had been dissected from surrounding tissue and packed off. It was closed with hemostats and packed off with gauze during the progress of the procedure. Primary union occurred despite this theoretical contamination. In the final case (No 2508-45) the technique had not yet been developed to the point of routinely leaving the fibrous ring on the neck of the sac and the strangulated gut slipped out of the sac and into the abdomen during dissection. It was fortunately an early case. In this group also one patient died (No 290-43) a very obese 75 year old man with a strangulated umbilical hernia whose repair was done in the face of frank cardiac failure which had not responded to attempts to digitalize him rapidly.

The inherent safety of the method is indicated by Case 4900 46, a 62-year-old cardiac patient with persistent orthopnea resulting from repeated coronary arterial thromboses. The procedure was necessarily done in a semisitting posture, but was well tolerated, and the patient was up and walking in seven days and home, well, in nine days.

CONCLUSIONS

This method of repair of femoral hernia containing gangrenous bowel avoids contamination

- (1) by division of the inguinal ligament
- (2) by opening the abdomen above the inguinal ligament to see and deal with the structures entering the sac
- (3) by resection en bloc of the sac, the fibrous neck of the sac, and the contents, and
- (4) by primary aseptic anastomosis of the distended intestine above this obstruction to the empty bowel below

The McVay-Haukins modification of the Lotheisen hernioplasty with reconstitution of the inguinal ligament completes the procedures.

In ten cases patterned on this plan, two patients have died, one of the heart failure with which he came, and one of a ruptured aortic aneurysm. The others left well.

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END TO END ANASTOMOSIS OF THE ESOPHAGUS FOR ESOPHAGEAL ATRESIA

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DURING the past eighteen months I have had the opportunity of operating on twenty infants with atresia of the esophagus. In fourteen of these cases it was possible after closure of the tracheoesophageal fistula to perform primary anastomosis of the esophagus. One baby had an atresia of the esophagus without an associated tracheoesophageal fistula, a gastroesophagostomy was successfully performed. With the exception of the first baby in this series of fifteen patients there were no postoperative deaths*. Multiple stage operations consisting of ligation and division of the fistula, gastrostomy and marsupialization of the esophagus were necessary for the remaining five patients. Two of these are living.

A mortality rate of 6.6 per cent for primary anastomosis of the esophagus in babies with atresia is an improvement over the results reported in the literature^{1,2,4}. Changes in technique and in pre and postoperative care may be partly responsible for this. A considerable portion of the credit is due to earlier diagnosis of the anomaly on the part of pediatricians and attending physicians. Furthermore, the dangerous practice of giving barium orally in this type of obstruction is now less common so that aspiration pneumonia in these cases due to barium has been less than in the past.

Preoperative Care—Shortly after the infant with esophageal atresia is admitted to the hospital a small soft rubber No. 8 catheter with three holes in one end is passed through the nostril into the upper esophageal pouch (Fig. 1). Gentle constant suction on the catheter is used to remove saliva from the blind esophageal pouch. This reduces the danger from further aspiration of saliva while the patient is being prepared for operation. The infant is then placed in oxygen given fluids parenterally to correct dehydration and started on sulfadiazene and penicillin to help overcome or prevent infection.

Four to twelve hours after the initial parenteral fluids have been given a red blood count is taken and if this is below 4.5 million a small blood transfusion is administered. If the blood count is over 4.5 million plasma is given instead of blood. Under this therapy in eighteen to twenty-four hours the baby's temperature which is often elevated at the time of admission usually returns to normal and the pulse slows and improves in quality. While it is not advisable to rush into operation until the infant has been carefully and adequately prepared it is useless to delay operation beyond forty-eight hours after admission. Little additional improvement in the infant's condition will

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*One baby died of congenital heart disease at 3 months of age. Necropsy showed the esophageal anastomosis to be healed without a leak.

be gained by further delay and the likelihood of further aspiration pneumonia is increased.

Anesthesia—One operation in this series was done under local novocain infiltration. This was a baby with extensive pneumonia, congenital heart disease, imperforate anus and perineal fistula. The pneumonia resulted from barium having been given by mouth in an attempt to make a diagnosis prior to admission to the hospital and the subsequent aspiration of considerable amounts of this irritating material. A primary anastomosis of the esophagus was performed. The baby made a slow recovery. At a later date anoplasty was performed under local anesthesia.



Fig. 1—Roentgenogram of patient with catheter in place in the upper esophageal pouch. A small amount of lipiodol has been injected through the catheter outlining the blind end of the upper segment.

Local novocain was also used as the anesthetic for part of a multiple stage procedure. This patient was a premature infant weighing 3 pounds 6 ounces. Anastomosis was not considered feasible as the segments were too far apart. Therefore the fistula was ligated and divided. The baby stood the procedure well. On the following day gastrostomy was performed under local novocain infiltration and cyclopropane was given for marsupialization of the esophagus immediately following the gastrostomy. A good recovery was made and the baby weighed 8 pounds 10 ounces at 6 months of age. (The remaining four patients subjected to multiple stage procedures were operated upon under cyclopropane anesthesia.)

In both patients operated upon under local anesthesia the infants were considerably disturbed and expended a great deal of energy. On the other hand we have seen no ill effects from light anesthesia with cyclopropane and the surgeon's work is facilitated.

Fourteen anastomoses of the esophagus have been performed under cyclopropane anesthesia with atropine as the only preoperative medication. Preoperative morphine has been discontinued because of the marked respiratory depression which it causes during cyclopropane anesthesia in infants.

Operative Approach—Immediately before operation a cannula is placed in an ankle vein, and blood is given during the procedure. More blood is lost than is usually appreciated, and adequate replacement is of great importance for a smooth operative course.

In all twenty cases a retropleural approach was used. In the first seven, a short segment of the third and fifth ribs and a long segment of the fourth rib were removed on the right side as far posteriorly as possible. In the last thirteen cases of this group, 15 cm sections of the third, fourth, fifth, and sixth ribs were resected, thus gave a better exposure than in the earlier cases. Remarkably little respiratory embarrassment was observed postoperatively, in spite of resecting part of four ribs. In one case roentgen examination two weeks after operation showed that new bone had bridged the gaps in the resected ribs.

Leaks in the anastomosis, when the approach is made retropleurally, are not necessarily fatal, as a fistula develops which drains through the wound and no fluid or air collects in the pleural cavity. In three cases at the Children's Hospital, not in this series, such fistulas have closed and the infants made good recoveries. This has also been the experience of Haight¹ in some of his cases. One baby in this series developed a fistula two weeks postoperatively. It was small, and closed spontaneously in about one week.

Once the mediastinum is entered by freeing the pleura from the thoracic cage, and ligating and dividing the azygos vein, the tracheoesophageal fistula can often be visualized. This structure is adjacent to the vagus nerve. In the Type III (of Ladd²) the fistula enters the back of the trachea and is readily identified. More difficulty will be encountered in exposing Type IV, where the fistula enters the carina and therefore is deeper in the mediastinum. Type III is by far the most common anatomic arrangement seen in this anomaly.

End to End Anastomosis of the Esophagus—The problem in making an end-to-end anastomosis is to overcome the distance between the upper and lower esophageal segments. In order to secure the maximum length to the lower portion of the esophagus the fistula is divided close to the trachea. As the fistula is being cut, the tracheal opening is closed by a running fine silk suture (Fig. 2). By this method there is never a large opening in the trachea during division of the fistula, and the maximum length of the lower part of the esophagus is obtained.

Not more than 2 cm. of the lower esophagus should be freed, as the blood supply is poor and ischemia of the end is easily produced. This may lead to necrosis of part of the wall or the impaired blood supply may prevent proper healing at the anastomosis.

In suturing the esophagus it is essential to avoid or reduce to a minimum the tension on the suture line. Furthermore, the anastomosis must be water tight as the baby will swallow saliva shortly after the end of the operation. Most anastomoses, except in this series, have been performed by the method of

Haight This method uses two rows of silk sutures telescoping the lower esophagus into the upper esophagus. No additional sutures are used to reduce the tension on the suture line.

In the present series a somewhat different technique has been employed. Because of the friable character of the lower esophageal segment it must not be depended upon to carry any tension. The upper pouch is in comparison a sturdy structure due to hypertrophy. Furthermore it has an excellent blood supply most of which originates high in the neck. Therefore it is

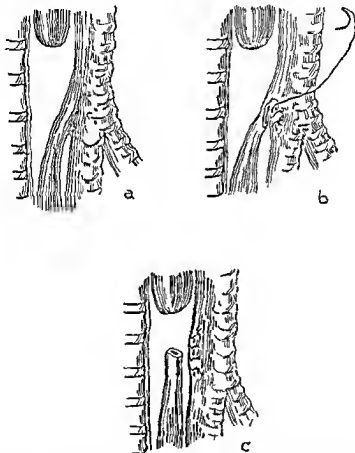


Fig. 2—(a) Schematic drawing of the relationship of the upper esophageal blind pouch, the tracheoesophageal fistula and trachea. (b) The fistula is partially divided and the tracheal side partially closed with a running fine silk suture. (c) The tracheal opening is shown closed. A second continuous suture has been used to turn in and reinforce the first suture layer.

possible to free the upper pouch high into the neck and thus gain considerable length. Because of the thickened wall of the upper pouch traction sutures placed through its muscular coats and submucosa are able to carry a considerable amount of tension. The traction sutures are then passed through the fibrous perivertebral fascia. When these are tied the upper esophageal pouch is

pulled down into the chest and tension on the suture line is reduced. By the use of these traction sutures, gaps of 4.5 cm. have been successfully overcome. In addition, such sutures will prevent motion at the suture line, and thus encourage healing (Fig. 3).

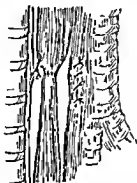


Fig. 3—Drawing showing the completed anastomosis with tension suture in place.

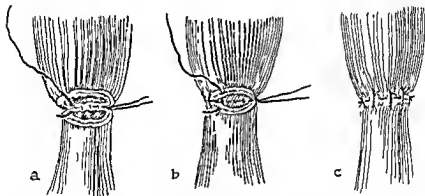


Fig. 4—(a) The anastomosis is started with a row of interrupted fine sutures through the muscular coats of the two esophageal segments. (b) A second row of fine interrupted sutures is placed to approximate the mucosa. (c) The anastomosis is completed with a row of silk sutures in the muscular coats anteriorly.

The making of the anastomosis itself is time consuming. First, a row of fine interrupted sutures is placed posteriorly through the muscular coats of the esophageal ends. A second row is then placed through the mucosa of the two ends to approximate this layer. The anastomosis is finished by completing the first row of interrupted silk sutures, to the muscular coats of the ends of the esophagus. This type of suture does not turn in a diaphragm, which is an advantage because the lumen of the lower esophagus is small (Fig. 4). The suture used is 5/0 silk on half circle atraumatic needle.

Passing the nasal catheter into the lower esophageal segment makes the anastomosis more difficult to perform. To insert the catheter into the lower esophageal segment after the anastomosis has been completed may damage the suture line. As soon as the operation is completed, the catheter, which has

remained in the upper pouch is removed. Leaving it in place postoperatively promotes pulmonary infection, and exudate along the tube in the nasopharynx may produce tracheal obstruction.

A small rubber drain extending down to the anastomosis is left in place in the wound for four days. In this group of fifteen patients with primary anastomosis of the esophagus, one leak of the esophageal anastomosis occurred. This took place two weeks postoperatively and the small fistula closed in one week.



Fig. 3.—Photograph showing feeding being dripped into gastrostomy. Note the sugar nipple used to maintain the infant's willingness to take food by mouth.

Postoperative Care—In the postoperative care the problem is to supply these infants with proper fluids and adequate protein and calorie intake, to forestall generalized edema which is a common and serious complication. Edema is due to a variety of causes, chief of these being the low protein reserve in newborn infants, excessive fluids, particularly saline solution, low caloric and inadequate protein intake and infection. If edema develops, the suture line is endangered by the swelling.

Oral feedings can be assimilated as soon as the anastomosis has been completed, but to give them on the fourth to eighth postoperative days is danger

ous, for the anastomosis is *weakest during that period*. Accordingly, it is felt that the wisest course is to *postpone feedings by mouth until the anastomosis is well healed*.

For this reason, on the day following the primary anastomosis a Stamm gastrostomy is performed, using *10 cc novocain anesthesia*. Eight hours after operation fluids are given *via the gastrostomy*, and in eighteen hours a dilute formula is started. This is brought up to full nutritional requirements in



Fig. 1. Roentgenogram of lipiodol in esophagus three weeks after anastomosis of the esophagus.

forty eight to seventy two hours depending on the condition of the patient. The feedings are at two hour intervals at first and are dripped in slowly through a Murphy drip. If given too quickly vomiting may take place and this is a severe strain on the esophageal anastomosis (Fig. 5).

During the two or three days after operation before a full diet is possible daily infusions of blood and plasma are given.

By such a regimen a reasonable protein and caloric requirement is soon made available to the infant. If a gastrostomy is not performed and all liquids are parenteral the fluid problem is difficult and a good protein intake cannot be supplied in the first few postoperative days when it is most essential.

In spite of all protective measures most of the infants become more or less edematous probably due to low serum protein. Concentrated albumin given intravenously has proved to be an invaluable aid in combating this distressing edema.

On the tenth postoperative day providing there have been no complications one half ounce of sterile water is given by mouth every two hours. If this is well tolerated a part of the formula is then given orally, and gradually increased until in two or three days all feedings are taken by mouth.



Fig 7.—Photograph of two children reported in this series. The baby on the left is 6 months old and the child on the right is 8 months old.

In only one of these infants has a stricture of the esophagus developed which required dilatation. This was an unusual case with atresia of the terminal ileum as well as atresia of the esophagus and tracheoesophageal fistula. The fistula was divided by a transpleural approach and the ileal atresia was corrected by a Mikulicz type of procedure. One month later a primary anastomosis of the esophagus was made by a retropleural approach. There was considerable scarring of the lower segment of the esophagus and therefore it was not surprising that esophageal dilatations were required in this case. No other patient in this series has required dilatation. By roentgen examination (Fig 6) some of these infants show fairly marked strictures. However as long as the formula is well taken dilatations are not necessary (Fig 7).

SUMMARY OF CASES

R. M. (996099) was admitted Aug. 4, 1945. This 9-day-old baby boy, weighing 5 pounds 6 ounces was admitted with a diagnosis of tracheoesophageal fistula and atresia of the esophagus. Examination revealed extensive pneumonia and marked generalized edema. On the following day the fistula was divided and an end-to-end anastomosis of the esopha

gus performed. A nasal tube was kept in place through the anastomosis, and feedings were given through the tube postoperatively. The baby had cyanotic attacks, respiration became labored, and he died on the second postoperative day. Respiratory troubles were apparently augmented by the nasal tube and in all subsequent cases its use has been omitted.

Necropsy demonstrated extensive pneumonia, pulmonary infarcts, and some mediastinitis. The anastomosis was intact. The fact that this child did not reach the hospital until the ninth day of life was undoubtedly a factor in his death.

L C (297981) was admitted Sept 19 1945. At 4 days of age this 3 pound baby girl with atresia of the esophagus and tracheoesophageal fistula was admitted to the surgical service of the Children's Hospital. The infant's general condition was fair, examination revealed a systolic murmur, thought to be due to a septal defect. End-to-end anastomosis of the esophagus was performed, followed by a gastrostomy two days later. On the tenth postoperative day small portions of feedings were commenced orally, and four days later all feedings were by mouth. She was discharged on the twenty-first hospital day.

The congenital malformation of the heart is associated with slight cyanosis on exertion but has not interfered with the normal growth and development of the child, who is now 15 months old.

S K (298870) was admitted Oct 19, 1945. This 3 day-old premature male infant weighing 4 pounds 4 ounces, had a mediastinal exploration for atresia of the esophagus and tracheoesophageal fistula. Closure of the fistula and an end-to-end anastomosis of the esophagus were performed. Gastrostomy was carried out the following day. The postoperative course was complicated by severe pneumonia. By the tenth postoperative day he had improved and a part of the feedings were started by mouth. He was discharged taking all feedings orally on the thirty-fourth postoperative day, and has continued to do well at home.

L H (304470) was admitted May 5 1946. At 5 days of age this baby girl weighing 6½ pounds was admitted to the Children's Hospital with a diagnosis of atresia of the esophagus and tracheoesophageal fistula. On the following day, under cyclopropane anesthesia, the fistula was closed and an end-to-end anastomosis of the esophagus made. Two days later a gastrostomy was performed under local anesthesia. Feedings were given via gastrostomy until the tenth postoperative day, when portions of feedings were started orally. The infant was discharged, taking all feedings by mouth, on the nineteenth hospital day.

D G (304447) was admitted May 9 1946. This 5 pound 10 ounce baby girl had excessive, tenacious mucus and regurgitations of fluid taken by mouth. A diagnosis of esophageal atresia was made and the child admitted to the Children's Hospital at 3 days of age. In spite of extensive pneumonia, an operation, consisting of division of the fistula and an end-to-end anastomosis of the esophagus, was performed. On the third hospital day gastrostomy was carried out under local anesthesia. For one month the baby was in a precarious condition because of the pneumonia. After this she improved, and was discharged on the sixty-sixth hospital day, weighing 8 pounds 1 ounce. She has continued to do well at home.

D Q (304556) was admitted May 12 1946. This 2 day-old baby boy, weighing 4 pounds had in addition to a tracheoesophageal fistula and atresia of the esophagus, an atresia of the terminal ileum. Through a right transpleural approach the tracheoesophageal fistula was divided and closed. An abdominal incision was then made during the same operation, a Mikulicz resection of the terminal bulbous ileum proximal to the atresia was done and a spur made between the ileum and colon. A malrotation of the cecum was also corrected and a gastrostomy performed. The baby did well and nineteen days later the ileostomy was closed.

An end-to-end anastomosis of the esophagus was performed five weeks after admission through a right retropleural approach. The patient was discharged on the fiftieth hospital day, taking all feedings orally. Three dilatations of the esophagus have been necessary in the six months after operation, none have been necessary in the past four months.

A D (306133) was admitted June 1, 1946. This 5½ pound baby girl was brought to the Children's Hospital at 2 days of age, because of atresia of the esophagus and tracheoesophageal fistula. On the day following admission the fistula was closed and an end to end anastomosis of the esophagus performed. A gastrostomy was made on the next day. There were no postoperative complications, and partial feedings by mouth were started on the twelfth postoperative day. She was discharged, taking all feedings orally, on the twentieth hospital day. Three days later she was readmitted because of vomiting. She was given all feedings by gastrostomy for twenty four hours, then gradually oral feedings were resumed. The baby did well and has continued to do so at home.

J W (307687) was admitted July 28, 1946. This 2 day old male infant weighing 5 pounds 7 ounces was admitted to the Children's Hospital and a diagnosis of atresia of the esophagus and tracheoesophageal fistula was made. The baby was in good condition and twenty four hours after admission the fistula was closed and an end to end anastomosis of the esophagus performed. A gastrostomy was performed the following day. The baby did well and small amounts of fluid were given by mouth on the thirteenth postoperative day. On the sixteenth hospital day the baby was discharged from the hospital, taking all feedings by mouth.

Three days later the baby was readmitted because of vomiting. This subsided after admission and recurred only occasionally until three weeks later, when it became projectile. A pyloric tumor could be palpated and a diagnosis of hypertrophic pyloric stenosis was made. Pyloromyotomy was performed. The baby has gained steadily since discharge.

J H (307093) was admitted Aug 11 1946. At 5 days of age this 6 pound baby boy had a mediastinal exploration for atresia of the esophagus and tracheoesophageal fistula. The fistula was divided and, in spite of the segments being 15 cm apart, an end to end anastomosis was performed. The postoperative course was complicated by a severe enteritis. This improved after ten days and the child then made a good recovery. He was discharged home on the twenty sixth postoperative day, taking all feedings by mouth.

C St G (308779) was admitted Sept 2, 1946. Because of regurgitation of all fluid offered this 2 day old, 5 pound 15 ounce baby girl was given barium by mouth and an atresia of the esophagus demonstrated. On the following day she was admitted to the surgical service of the Children's Hospital with extensive pneumonia, and there was a loud cardiac murmur indicating congenital heart disease. An imperforate anus, with a small perineal fistula, was also present.

Because of the extremely poor condition of the infant, the mediastinum was explored under local anesthesia, the tracheoesophageal fistula divided and an end to end anastomosis of the esophagus performed. In spite of the infant's poor condition, a gastrostomy was made under local anesthesia the following day. The postoperative course was stormy because of extensive pneumonia and heart disease. Frequent bouts of tachycardia were not well controlled with digitalis.

One month postoperatively anoplasty was performed under local anesthesia. A slow recovery was made, and the patient was discharged on the forty fifth hospital day, taking all feedings by mouth. The baby was readmitted to the Children's Hospital because of pneumonia and congenital heart disease and died at 3 months of age. Necropsy demonstrated the esophageal anastomosis and the closed tracheoesophageal fistula to be healed. There was extensive pneumonia and a large interventricular defect in the heart.

J G (309512) was admitted Sept 12 1946. This 3-day old baby boy, weighing 6 pounds 4 ounces was admitted to the Children's Hospital with a diagnosis of atresia of the esophagus and tracheoesophageal fistula. On the day following admission an end to end anastomosis of the esophagus was made and the fistula divided. The next day a Stamm gastrostomy was established under local anesthesia and fluids were given through this, twelve hours postoperatively. The baby did well and was started on small oral feedings on the tenth postoperative day. He was discharged twenty days after admission, taking all feedings by mouth. Five months later the baby weighed 15 pounds.

M M (309536) was admitted Sept. 16 1946. This 5 pound 5 ounce baby boy was admitted to the Children's Hospital at 5 days of age. Roentgen studies revealed an esophagus

phageal atresia without a tracheoesophageal fistula. Usually in such cases there is absence of a great part of the lower esophagus, making an end-to-end anastomosis of the esophagus impossible. Through a left transpleural approach the diaphragm was opened and the stomach brought into the chest and anastomosed to the upper esophageal pouch. This was possible as the pouch was unusually low in the chest, extending to the bifurcation of the trachea.

Feedings by mouth were started on the first postoperative day, and the baby did well except for some diarrhea. He was discharged on the eighteenth postoperative day, taking all feedings by mouth. He has done well at home weighing 9 pounds at 3 months of age. Feedings are small in amount and have to be given every three hours.

J. W. (311220) was admitted Oct. 26, 1946. This baby boy was admitted to the Children's Hospital at 3 days of age, weighing 7 pounds 13 ounces, with a diagnosis of esophageal atresia and tracheoesophageal fistula. The following day an end-to-end anastomosis of the esophagus was made and the fistula closed. Twenty-four hours later a Stamm gastrostomy was performed. The baby did well, and on the tenth postoperative day small feedings by mouth were started. No fistula developed. He was discharged, taking all feedings by mouth on the eighteenth hospital day.

R. S. (311426) was admitted Nov. 10, 1946. This 6 pound 6 ounce baby boy was admitted to the Children's Hospital with a diagnosis of imperforate anus, at 1 day of age. It was noticed on the surgical service that there was excessive salivation. A soft rubber catheter passed through the nostril into the esophagus demonstrated an obstruction. A diagnosis of atresia of the esophagus and tracheoesophageal fistula, in addition to the imperforate anus, and rectovesical fistula, was made.

A sigmoidostomy and gastrostomy were performed under local anesthesia. Two days later the tracheoesophageal fistula was closed and an end-to-end anastomosis of the esophagus performed. The postoperative course was complicated by occasional vomiting due to the poor function of the colostomy. As the colostomy started to function well, the vomiting stopped.

R. B. (312406) was admitted Dec. 3, 1946. At 3 days of age this 5 pound 6 ounce baby boy had a mediastinal exploration with division of a tracheoesophageal fistula and end-to-end anastomosis of the esophagus. The following day a Stamm gastrostomy was done. The postoperative course was uncomplicated. Small oral feedings were begun on the tenth postoperative day. The infant was discharged on the eighteenth postoperative day, taking all feedings by mouth.

SUMMARY

A series of twenty patients with esophageal atresia that I have operated upon is reported. Fifteen patients had primary anastomosis of whom fourteen survived, five had multiple stage procedures and two of these survived one of whom has had an anterior thoracic esophagus completed and the second awaits esophagoplasty.

Pre and postoperative care are described. Details are given for an operative method for performing an end-to-end anastomosis of the esophagus.

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OPEN JUMP FLAP REPAIRS OF THE LOWER EXTREMITY

LIEUTENANT COLONEL BRADFORD CANNON, MAJOR CARL E. LASCHER AND
COLONEL JAMES B. BROWN (BY INVITATION)
ARMY OF THE UNITED STATES

THE large broad surface defects and extensive deep scars of the lower extremity which must be resurfaced with flaps for better covering or before successful deep surgery can be done present a difficult problem in securing adequate amounts of skin rapidly and by simple direct methods. The use of the open jump flap from the abdominal wall instead of a long tubed flap has reduced the time needed to complete a repair from many months to several weeks. By this method wider defects can be covered than with a tubed flap which is necessarily limited in its width. Thus a single flap has been used to cover the sole and sides of the foot. And in another patient a flap has been used to cover the whole anterior surface of the tibia. In some scars of the lower leg which might have been resurfaced with large local flaps a jump flap has been preferred because the procedure is more rapid, less hazardous and the results are more satisfactory.

The importance of removal of deep scar and restoration of adequate surface covering before bone, tendon and nerve repairs can be accomplished successfully has been emphasized before.^{1, 2} The bumps and blows to which the lower extremity and foot are exposed make adequate surface covering important even if no additional deep surgery is necessary. Consequently a simple direct method of repair is important.

The success of the open jump flap from the abdominal wall depends on the maintenance of a short broad pedicle throughout all stages of the transfer. Sufficient mobility of the leg, shoulder and body to permit this shifting of the carrier arm into juxtaposition with the leg or foot is essential. The transfer has been done successfully to the sole of the foot, to the leg at the level of a stiff knee and to other parts of the lower extremity. Selection of the ipsilateral or contralateral arm depends on which will accomplish the result with minimal discomfort in the cramped position. The contralateral arm may be preferred for large foot repairs. The radial side of the arm is generally used to carry the flap but the ulnar side may be better in certain repairs such as the lateral aspect of the thigh. An excess of at least one third in the size of the flap is allowed to compensate for shrinkage. One of the virtues of the open jump flap is that an adequate excess can be transferred. Failure to provide enough skin defeats the purpose of the procedure and may necessitate a second flap.

phageal atresia without a tracheoesophageal fistula. Usually in such cases there is absence of a great part of the lower esophagus, making an end-to-end anastomosis of the esophagus impossible. Through a left transpleural approach the diaphragm was opened and the stomach brought into the chest and anastomosed to the upper esophageal pouch. This was possible as the pouch was unusually low in the chest, extending to the bifurcation of the trachea.

Feedings by mouth were started on the first postoperative day, and the baby did well except for some diarrhea. He was discharged on the eighteenth postoperative day, taking all feedings by mouth. He has done well at home, weighing 9 pounds at 3 months of age. Feedings are small in amount and have to be given every three hours.

J W (311223) was admitted Oct 26, 1946. This baby boy was admitted to the Children's Hospital at 3 days of age, weighing 7 pounds 13 ounces, with a diagnosis of esophageal atresia and tracheoesophageal fistula. The following day an end-to-end anastomosis of the esophagus was made and the fistula closed. Twenty-four hours later a Stamm gastrotomy was performed. The baby did well, and on the tenth postoperative day small feedings by mouth were started. No fistula developed. He was discharged, taking all feedings by mouth on the eighteenth hospital day.

R S (311426) was admitted Nov 10, 1946. This 6 pound 6 ounce baby boy was admitted to the Children's Hospital with a diagnosis of imperforate anus, at 1 day of age. It was noticed on the surgical service that there was excessive salivation. A soft rubber catheter passed through the nostril into the esophagus demonstrated an obstruction. A diagnosis of atresia of the esophagus and tracheoesophageal fistula in addition to the imperforate anus, and rectovesical fistula, was made.

A sigmoidostomy and gastrotomy were performed under local anesthesia. Two days later the tracheoesophageal fistula was closed and an end-to-end anastomosis of the esophagus performed. The postoperative course was complicated by occasional vomiting due to the poor function of the colostomy. As the colostomy started to function well, the vomiting stopped. The infant was discharged on the twenty-second postoperative day, taking all feedings orally. He was readmitted three days later because of a fistula from the esophagus to the back. This closed in seven days and has remained closed since that time (three months).

B B (312406) was admitted Dec 3, 1946. At 3 days of age this 5 pound 6 ounce baby boy had a mediastinal exploration with division of a tracheoesophageal fistula and end-to-end anastomosis of the esophagus. The following day a Stamm gastrotomy was done. The postoperative course was uncomplicated. Small oral feedings were begun on the tenth postoperative day. The infant was discharged on the eighteenth postoperative day, taking all feedings by mouth.

SUMMARY

A series of twenty patients with esophageal atresia that I have operated upon is reported. Fifteen patients had primary anastomosis of whom fourteen survived, five had multiple stage procedures and two of these survived one of whom has had an anterior thoracic esophagus completed and the second awaits esophagoplasty.

Pre and postoperative care are described. Details are given for an operative method for performing an end-to-end anastomosis of the esophagus.

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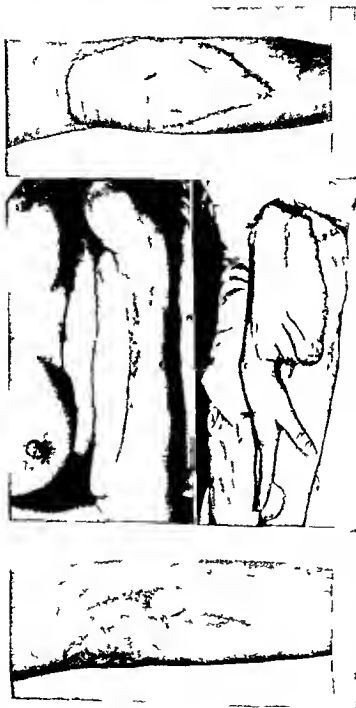


Fig 2—The u facing of f ont of knee with an open jump flap as a preliminary to r pa r of quadriceps t ndon completed with s x operations in twelve weeks

TECHNIQUE

An incision longer than the defect of the leg or foot is made on the radial or ulnar side of the forearm selected as the carrier of the jump flap. With short perpendicular incisions at either end a long narrow flap is elevated. A direct abdominal flap of corresponding size is prepared at a suitable place on the abdominal or chest wall. The flaps are overlapped and sutured together. Any underlying raw surface on the abdominal wall is grafted.



Fig 1.—Resurfacing of sole of foot with open jump flap. Mid thigh amputation of the other leg makes cross leg flap impossible. Repair was accomplished by flap carried on the opposite forearm, completed with eight operations in sixteen weeks.

The delay of the remainder of the flap or 'pancake' outlined on the abdominal or chest wall is usually completed in two or three stages, the first after about two weeks or more and the others at about weekly intervals. The delay consists in the partial severing of the normal blood supply to the flap at each stage. At the first stage, incisions are made along one or two borders and the flap undermined. At the next stage the remaining borders are cut and the undermining completed. A third stage is necessary only if the flap is too large to permit complete delay in two procedures. After each of the operations the incisions are sutured so that there is no exposed raw surface. Resilient pressure dressings with cotton waste for support and hemostasis are essential after each of these procedures to insure primary healing. Adhesive strips are adequate for fixation but an encircling bandage may be used. Either one allows ready access to the wound for inspection of the flap and change of dressings.

The prepared flap is now detached from the abdominal wall and the bed from which it came is usually covered with a split thickness graft. The scar on the lower extremity or foot is dissected free removing all deep scar tissue until an adequate minute blood supply is present. The back rest of the operating table can be elevated so that the leg and the arm are brought together. When a suitable position has been established by adjusting the table and supporting the patient with sandbags or pillows the flap is carefully and accurately sutured in place. If the pedicle of the flap is needed to cover part of the scarred surface the scar is not removed completely until a final adjustment is made. A plaster cast is usually preferred to maintain position of the body arm and leg at this stage but adhesive fixation may prove satisfactory. The fixation does not allow ready access to the wound but full support of the patient through this period makes him more comfortable.

In the transfer of the flap to the leg or foot a combination of local infiltration anesthesia for elevating the flap and a low spinal anesthetic for dissection of the leg and cutting a free graft to cover the donor area has proved more suitable than general anesthesia or local infiltration alone. With the patient's cooperation firmer fixation can be established more comfortably and in a more suitable position.

Two delays usually suffice in detaching the flap from the arm. Adjustment of the flap on the leg or foot and resuture of the narrow flap in the arm may be done at the same time that the flap is cut free or may be postponed until later.

It has been possible to complete the procedure from the first operation until the final adjustment in as little time as ten weeks. Some of the larger flaps however have taken twelve to sixteen weeks. The arm is attached to the abdominal wall for three to five weeks and to the leg for another three to five weeks and the final adjustment is done one to three weeks later.

COMMENT

The use of open jump flaps from the abdominal wall has made possible the completion of repairs of large surface defects of the lower extremities and



Fig. 3—The facing of the vent of over the anastomosis, the flap from the anastomosis, the flap from the anastomosis, the flap from the anastomosis, the flap from the anastomosis.

ONE STAGE PUSH BACK OPERATION FOR CONGENITAL INSUFFICIENCY OF THE PALATE

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(From the Department of Surgery, New York Hospital and Cornell University Medical College)

THE classic work of Dorrance and Bransfield^{1,2} on the anatomy and physiology of the palate and their description of the technique of the push back operation have served to establish the principles of surgery directed toward the correction of imperfect speech in cases of congenitally short palate. The operation is performed in two stages. At the first operation the mucoperiosteal flap is elevated, the palatine arteries are divided, and a split skin graft is sutured to the periosteal surface of the mucoperiosteal flap, which is then sutured back to its original position. Three to ten weeks later, when collateral circulation is established, the mucoperiosteal flap is elevated and is dislocated posteriorly so that the distance between the soft palate and the posterior pharyngeal wall is diminished sufficiently to allow for physiologic closure of the velopharyngeal sphincter. Although the functional results are good in a high percentage of cases following the use of this technique, the objection to it lies in the fact that two operations are necessary. Multiple operations are known to favor the development of fibrosis of the soft palate with consequent limitation of mobility which in some cases is reflected in imperfect speech. Cognizant of this problem, Brown³ described his single stage operation for elongation of the congenitally short palate. In this procedure the mucoperiosteum of the hard palate is elevated as a direct flap and immediately set back. The palatine arteries are preserved. The posterior dislocation of the flap and the soft palate is accomplished by "careful loosening of all tissue around the artery, gently stretching it from the foramen and if necessary, carefully cutting it away from the palatal flap." Brown stated that the contracture resulting from healing on the raw surface of the mucoperiosteal flap which is exposed in the nasopharynx, does not seem great enough to warrant the use of a skin graft. In commenting upon this technique, Dorrance and Bransfield have pointed out that if sufficient lengthening of the palate is obtained the palatine arteries must of necessity be acutely kinked. It has been my experience that, in many cases, free backward dislocation of the palate cannot be obtained by the method described by Brown.

Interest in this problem led to the dissection of anatomic specimens of the palatine bone. It was determined that the course of the palatine artery through the pterygopalatine canal invariably is downward and forward. Fig. 1 shows an artist's sketch of this relationship. Viewed from above and from in front the descending palatine artery meets the horizontal plate of the palatine bone at an obtuse angle of approximately 135 degrees. Moreover, detailed study of the regional anatomy demonstrates that the contents of the pterygopalatine canal

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foot in a much shorter time than by other remote methods. The local double pedicle or "slash" flap and the delayed local flap are more direct methods, but the size of the defect to be covered is limited and future deep surgery may be complicated by the scar on the leg. Open jump flaps are practically not limited in their width or length and the hazard of their transfer is reduced because at all times a broad attachment to the arm is maintained. A total of twenty two open jump flaps have been done with success in all but one instance. In this case, there was a narrow marginal loss.

In the late care of all flaps, especially those covering a weight bearing surface, daily inspection is important because of the possibility of local necrosis and ulceration from trauma or burns in the insensitive flap. Return of sensation in all flaps is a slow process requiring months and occasionally years for complete regeneration. The rate of regeneration depends on the location of the flap and the adjacent or underlying nerve supply. Regeneration of the sole of the foot is therefore far slower than the thigh. In this group of recent flaps, only partial regeneration can be reported.

SUMMARY

The open jump flap from the abdominal wall in repairs of the lower extremity and foot is described.

Success of the open jump flap depends on the maintenance of a short broad attachment to the forearm throughout all stages of the transfer.

Large repairs by this method can be completed more rapidly and with more satisfactory results than by other remote methods.

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vascular bundles and the soft palate before and after reposition by this technique. The palate is depicted as at rest in this diagrammatic sketch. In preparation for the osteotomy the nasal mucosa is divided at the junction of hard and soft palate. The osteotomy is performed with a small chisel. The neurovascular bundle is retracted laterally as the posterior bony shelf is cut medially and then is retracted medially as it is cut laterally. A thin plate of bone 3 to 4 mm. in width and 1 to 1.5 cm. in vertical dimension is removed. Fig. 4 is a sketch of the palatal region. On the left side the posterior bony wall of the canal has been removed. On the right side the dotted lines indicate the point at which the chiseling is started. After the osteotomy is completed the palate is dislocated posteriorly so that the soft palate touches the posterior pharyngeal wall. Sutures are placed to hold the anterior margin of the mucroperiosteal flap to the fringe of the nasal mucosa attached to the hard palate (Fig. 4). In cases in which there is a bony cleft the palate may be split in a horizontal plane (as recommended by Brown) so that an opening into the nose is avoided.

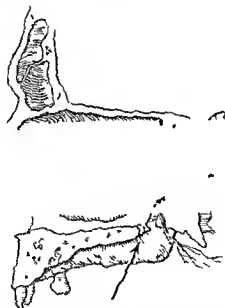


FIG. 4.—Art. is sketch of sagittal section of bones of the face and mouth. In this specimen the posterior wall of the bony pterygopalatine canal has been removed and the descending palatine artery concomitant vein and the anterior branch of the palatine nerve are being brought back so that the angle at which they meet the horizontal plate of the palatine bone when it is set from in front and above is an acute angle of approximately 45 degrees.

The technique for a one stage push back operation which has just been described has been carried out in sixteen patients without injury to the palatine artery. These patients have been followed for periods of time varying from one to fourteen months. Following operation speech training has been emphasized. The expert work of Est. D. Freud speech trainer at the plastic surgery clinic of The New York Hospital has been an invaluable aid not only in training these

include not only the descending palatine artery but also concomitant veins and the anterior branch of the palatine nerve, the fibers of which are derived from the sphenopalatine branches of the maxillary nerve. This nerve supplies the mucous membrane and the mucous glands of the hard palate and the alveolar process. Both the right and the left anterior palatine nerves send branches to both sides of the palate. In anatomic specimens it is a simple procedure to chip away the thin bone which forms the posterior wall of the pterygopalatine canal, thus completely freeing the small neurovascular bundle. Its easy posterior dislocation is shown in Fig 2. Viewed again from above and in front the angle at which the palatine neurovascular bundle meets the plane of the horizontal plate of the palatine bone is seen to be an acute angle of approximately 45 degrees.



Fig 2. A sketch of sagittal section of the bones of the face and mouth. The dashed line indicates the path of the palatine nerve which coats the descending of the palatine nerve. Viewed from above and in front the angle at which the palatine neurovascular bundle meets the plane of the horizontal plate of the palatine bone is seen to be an acute angle of approximately 45 degrees.

Fig 3 shows the relative positions of the maxillary artery and the maxillary nerve.

stage Fig 3 shows the relative positions of the maxillary artery and the maxillary nerve.

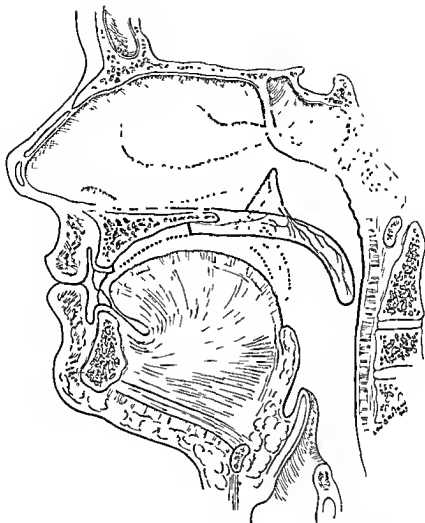


A



B

Fig 5 (For legend see opposite page)



back
wall of
soft
palate
bony
palate
muscle

anatomy involved in the one stage push
back of the congenitally short palate. The
mucosa at the junction of hard and
the bony palatine canal allow
the mucoperiosteal flap and the soft
of the small palatine neurovascular
lateral and superior extensions of the

Fig. 3—A X ray visualization of the position of the congenitally short palate as the patient tries to pronounce *k*. The tongue the posterior pharyngeal wall and both surfaces of the soft palate are outlined by an opaque ointment made of bismuth and petroleum jelly. In this case the distance between soft palate and posterior pharyngeal wall before operation was 2.5 cm. When trying to say *k*, the patient pronounced *ka* with strong nasalization of the sound.

B X ray visualization as the patient pronounced *k* after the one-stage push back operation had been done as outlined in this report. Note that the soft palate has been lengthened so that it now effectively closes the velopharyngeal sphincter. With the palate at rest the distance from posterior extension of soft palate to posterior pharyngeal wall was only 7 mm. The pronunciation of the posterior linguopalatal was normal.

THE REPARATIVE SURGERY OF SGFT PART WOUNDS

SAMUEL P. HARMISON, M.D., PITTSBURGH, PA

THE division of wartime surgery into initial, reparative, and reconstructive phases by Edward D. Churchill has been a very useful one. It has clarified considerably the study of war wounds in that each phase may be appraised separately, in keeping with the fact that different surgeons worked exclusively, for the most part, in one or the other situation, and few had an opportunity to serve effectively in more than one. This paper deals with the reparative phase only, that period which begins as soon as the soldier is evacuated following initial surgery, and ends when he is returned to duty in the theater, or evacuated to the Zone of the Interior for reconstructive surgery or prolonged convalescence. In the majority of cases the reparative phase concerns the early closure of wounds of soft parts and the rapid rehabilitation of the soldier but in a considerable number it means early closure of extensive injuries to facilitate later reconstructive work.

The Twenty first General Hospital* was fortunate in being the first general hospital to function in North Africa remaining there a year, in serving for nine months in the Italian theater, and then for ten months in eastern France. Thus it was possible to watch the changes in the treatment of wounds and to carry out early improvements in management. During the North African campaign the patients were received many days after wounding, usually after being evacuated through several installations. Most of the wounds were granulating and contaminated, if not actually infected. Scar disability, and invalid reactions were all too frequent. All surgeons recognized the necessity for earlier closure and tried out various methods. In Italy real advances were made. In this geographically small theater lighter casualties were speedily evacuated (one to four days) to general hospitals where early closures were extensively tried and studied, leading to certain well defined principles in the technique which were included in the directives of the Surgical Consultant for the theater. Shorter hospitalization, lessened disability, better morale, and decreased nursing care were the results. In France, during the third year abroad with even larger number of patients, wound closure on or before the fifth day became routine in almost every suitable case. This was made possible by developing special operating room techniques whereby five surgeons, one instrument nurse and five anesthetists could handle 100 cases for closure (suture and/or graft) in a five hour period (Fig 1).

Table 1 shows the material upon which this paper is based. The division of the data into countries serves to indicate the changing demands put upon the hospital as the war progressed. The experience is a large one and the table refers only to general surgery, it does not include the large number of orthopedic cases. Even though much has been written to date upon the sub

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*Washington University St Louis Mo

patients in the development of normal speech but also in the selection of cases for operation. At the present time eleven patients can be said to have normal phonation and enunciation while five are still taking speech training. This operative technique has been applied to an adult in only one case. Advantage was taken of the cooperative attitude of this 53 year old woman to obtain x-ray evidence of the effect of the operation. According to the method of Froeschels and Haudek,* the tongue, the posterior pharyngeal wall, and the two surfaces of the soft palate were coated (after cocaineization) with an ointment of bismuth and petroleum jelly. The positions of the soft palate before and after operation as the patient tried to close the velopharyngeal sphincter in pronunciation of the consonant "K" are shown in Fig 5.

SUMMARY

An additional operative step in the technique of the push back operation for congenitally short palate is described. This step consists of the removal of a portion of the posterior wall of the bony pterygopalatine canal thus permitting easy backward displacement of the mucoperiosteal flap and the soft palate. By this step the blood supply and innervation of the palate are preserved. The procedure permits satisfactory lengthening of the palate by a one stage operation. The operation may be applied to cases in which there is congenital insufficiency of the palate without cleft as well as to cases in which there is shortening of the palate in association with incomplete or complete clefts.

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Fig. 1—Operating room for delayed primary suture. One sterile nurse (right) supplies Mayo tables for five simultaneous operations two of which are seen. Fifty cases may easily be handled in a few hours by five surgeons.



Fig. 2—The upper wound represents a delayed primary closure (tenth day) this suture of the chest wall made possible the removal of a large intraplemonic foreign body through the lower thoracotomy wound at an early date.

TABLE I SURGERY OF FOOT-PAW WOUNDS*

	TOTAL	AFRICA (11 MO)	ITALY (9 MO)	FRANCE (MO)
Delayed primary and secondary closures	8443	111	2497	54
Débridements primary and secondary	571	43	19	331
Removal of foreign bodies	388	115	84	145
Split-skin grafts	421	60	16	196

*Figures refer to patients not wounds. General surgery only.

ject of wound closure it was felt that this large series due to the fact that the hospital worked intimately in all phases of the problem from the beginning was worth reporting. The outstanding impression obtained is that all surgical procedures became more and more simplified as time went on so that now a comparatively few principles can be set down to cover all the problems. This simplicity became apparent only after discarding by trial and error many involved and unnecessary innovations.

DRESSINGS

The requirements of a satisfactory dressing after initial surgery include several essential points. They must remain in place, prevent edema of the wound and surrounding tissues, allow secretions to be absorbed and afford a varying degree of splinting depending upon the wound. The inadvisability of the use of petrolatum gauze did not become apparent for some time not only as a packing (or better wick) in deep wounds and fractures but as a covering for surface wounds and burns as well. In Italy many French and French Colonial troops were received from a French evacuation hospital. French surgeons at that time did more extensive debridements than our surgeons and dressed the long wounds with plain gauze impregnated with an aqueous antiseptic. Four days later the dressings were noted to be totally bloodstained, quite hard and firmly in place. Upon removing them under pentothal in the operating room an exceedingly clean red wound without edema was apparent which, when drawn together simply with sutures, healed most kindly. The secretions of the wound had been absorbed into the dressing where they dried and transformed the gauze dressing into the equivalent of a light cast. In contrast were wounds dressed with petrolatum gauze; the outside of the dressings looked very clean but within were secretions dammed up behind the impervious inner layer of grease gauze and on the raw wound was usually a thin layer of gray fibrinous exudate. More and more frequently petrolatum gauze was discarded from various types of wounds until in the French theater dry fine mesh gauze was used as the exclusive innermost dressing for extensive granulating areas and burns and for the initial dressing on skin grafts. The granulation color and cleanliness of burns were striking. The essential improvement rested upon the facility with which plain gauze passed on the secretions into the bulk of the rest of the dressing.

At first it had been customary for the wound to be inspected at each stop in the evacuation of the soldier. The danger of this procedure soon became evident; contaminated wounds became infected with human pathogens where

where during busy periods five Mayo tables for five operating tables were kept supplied with essential instruments (from a common supply) by one sterile nurse. A graft simply required the addition of a knife and board to these tables. Following closure firm dressings of dry gauze were applied not to be changed until about the seventh day when in simple clean closures the sutures were removed and no dressing was reapplied. This last procedure helped the morale of the soldier rehabilitated him more quickly and saved dressings. No infections were seen as a result of it.

Thus the wound is managed entirely in operating rooms under aseptic conditions. Dressings become extremely simple when only the essential features are incorporated: initially dry fine mesh gauze next to the wound, bulky but firm outer dressings, splinting where necessary, one change of dressing only and that done in the operating room of the general hospital at the time of closure. An exceedingly valuable adjunct is the use of stockinet made into a single thickness by cutting it on the bias in a spiral fashion. This provides a roller outside dressing of any desired width and length which gives excellent pressure and splinting, follows the contours of irregular parts accurately, may be washed and reused, and does away with the necessity of adhesive fixation. It is superior to the commercial elastic bandage and is more comfortable when worn directly next to the skin. It is also much cheaper.*

WOUND CLOSURE

A study of closures more properly designated delayed primary closures was made in Italy in 1943 and early 1944. The following factors were noted in a very careful evaluation of 200 consecutive cases: (1) time in hours from receiving wound to the initial debridement; (2) time in days from initial surgery to closure; (3) size, depth, and position of wound; (4) number of dressings prior to reparative closure; (5) technique of closure (buried sutures, excision, partial excision or nonexcision of the wound, use or nonuse of local chemotherapy); (6) dry or wet dressings postoperatively; (7) anaerobic and aerobic cultures of the wounds immediately prior to closure; and (8) the surgeon performing the closure. The grading of the results purposely was very strict: four plus referred to per primam healing without redness or induration; three plus to the presence of redness but no induration or exudate; two plus to slight exudation of serum (or pus from a suture hole); one plus to partial separation of the wound edges or the necessity to remove sutures because of infection; zero to total separation or breakdown; and double zero to spreading infection with definite harm incurred. There were no wounds in the series in the zero and double zero category. There was no correlation whatsoever between the types of organisms obtained upon culture and the success or failure of the operation. Because of the small size of the series the only interesting figures are those obtained by grouping grades two plus, three plus, and four plus together representing satisfactory results (Table II). And

*First Lie tenant Eleanor B. Bakmeyer, A.N.C. suggested the substitute elastic bandage to us and our thanks go to her for the uncounted miles of stockinet which she cut on the bias.

before only saprophytes had been present the pressure upon the wound was lost and edema developed each dressing injured the raw wound beneath. The procedure was also a tax on time and supplies. Greater experience showed that trouble in a wound almost always showed up in one or more of the symptoms or signs of pain, tenderness, fever, or elevated pulse. With more rapid closures it became the rule not to disturb dressings in any way until the wound was inspected in the operating room on the fourth or fifth day after initial surgery with immediate closure in contemplation. Ward officers with the soldier's chart and the record of a twenty-four hour period of observation in their own hospital soon became expert in assessing a wound without exposing



Fig. 3. Simple equipment for skin grafting in use in Africa before regular knives were supplied. A bread knife and a suction box made from a tin can.

it holding back from the operating room those wounds that were too small for formal closure or those exhibiting spreading infections. Thus the original initial surgical dressing was in place in the operating waiting room of the general hospital where the sergeant and his crew mastered and trained in aseptic technique took down the dressing to the layer next to the wound, cleaned the area if indicated. On occasion to visualize the size of the defect, podermics were administered to the operating room by the corpsmen and the soldier was brought

where during busy periods five Mayo tables for five operating tables were kept supplied with essential instruments (from a common supply) by one sterile nurse. A graft simply required the addition of a knife and board to these tables. Following closure firm dressings of dry gauze were applied not to be changed until about the seventh day when in simple clean closures the sutures were removed and no dressing was reapplied. This last procedure helped the morale of the soldier rehabilitated him more quickly and saved dressings. No infections were seen as a result of it.

Thus the wound is managed entirely in operating rooms under aseptic conditions. Dressings become extremely simple when only the essential features are incorporated: initially dry fine mesh gauze next to the wound, bulky but firm outer dressings, splinting where necessary, one change of dressing only, and that done in the operating room of the general hospital at the time of closure. An exceedingly valuable adjunct is the use of stockinet made into a single thickness by cutting it on the bias in a spiral fashion. This provides a roller outside dressing of any desired width and length which gives excellent pressure and splinting, follows the contours of irregular parts accurately, may be washed and reused, and does away with the necessity of adhesive fixation. It is superior to the commercial elastic bandage and is more comfortable when worn directly next to the skin. It is also much cheaper.*

WOUND CLOSURE

A study of closures more properly designated delayed primary closures was made in Italy in 1943 and early 1944. The following factors were noted in a very careful evaluation of 200 consecutive cases: (1) time in hours from receiving wound to the initial debridement; (2) time in days from initial surgery to closure; (3) size, depth and position of wound; (4) number of dressings prior to reparative closure; (5) technique of closure (buried sutures, excision, partial excision or nonexcision of the wound, use or nonuse of local chemotherapy); (6) dry or wet dressings postoperatively; (7) anaerobic and aerobic cultures of the wounds, immediately prior to closure; and (8) the surgeon performing the closure. The grading of the results purposely was very strict: four plus referred to per primam healing without redness or induration; three plus to the presence of redness but no induration or exudate; two plus to slight exudation of serum (or pus from a suture hole); one plus to partial separation of the wound edges, or the necessity to remove sutures because of infection; zero to total separation or breakdown and double zero to spreading infection with definite harm incurred. There were no wounds in the series in the zero and double zero category. There was no correlation whatsoever between the types of organisms obtained upon culture and the success or failure of the operation. Because of the small size of the series the only interesting figures are those obtained by grouping grades two plus, three plus and four plus together representing satisfactory results (Table II). And

*First Lieutenant Eleanor Brinkmeyer, A.N.C., suggested this substitute elastic bandage to us, and our thanks go to her for the uncounted miles of stockinet which she cut on the

TABLE II STUDY OF 200 CASES OF WOUND CLOSURE*

	PER CENT SATISFACTORY	PER CENT UNSATISFACTORY
Local use of sulfanilamide	78	22
No local drug	97	13
Wounds less than 11 days old	91	9
Wounds more than 11 days old	78	22
Wet dressings postoperatively	96	4
Dry dressing postoperatively	79	21
"Surgeon factor"—lowest of 8 men	50	50
"Surgeon factor"—highest of 8 men	91	6

*See text for interpretation of results

of these figures only the remarkable "surgeon factor" is of significance, of the eight surgeons doing the closures, individual "satisfactory" results varied from 50 to 91 per cent! This finding naturally makes interpretation of the other variables impossible.

Directly related also to the success of closure was the surgeon factor at the initial débridement at the front. There was great variance in competence depending upon experience (both prewar experience and that obtained during the war), and the resulting difference in wounds constituted a most important observation. This variation in results depending upon the operator, an unexpected finding in the series, resulted in considerable skepticism in regard to reports of closure techniques unless done by one man exclusively.

In any event the over all value and high degree of success of early closures were established by all hospitals. With better evacuation and more experience the simple principles involved became apparent. These included the dressing technique already described, closure of the wound within five days by simple suture or graft without disturbing the wound itself in any way except to free gently the retracted skin edges. (The surrounding skin surface only was treated with an antiseptic.) Secondary wound excision, the local use of sulfonamides, moist buried sutures, petrolatum dressings—all were discontinued. Large wounds with considerable skin loss were sometimes undercut to obtain normal skin closure, and occasional flaps were swung to cover important areas, but simplicity gave the best results, and if excessive tension would result from direct suture split grafts were used freely.

Soft part wounds in the reparative phase were found to fall into three general categories: (1) those suitable for immediate closure on the third to fifth day, constituting about 80 per cent of the cases (Figs. 4, 5, A and B, and 7, A and B), (2) those in which débridement had been incomplete but in which there was no evidence of infection or cellulitis, and (3) those in which infection appeared to have the upper hand with cellulitis, induration, excessive suppuration, and considerable constitutional reaction. Wounds in the second category were redébride

(Fig. 6, A and B)

immobilization, and

True secondary closures in these cases were always uncertain, such as the

closures had been in Africa. Burns fell naturally into the second category since by redebridement, when demarcation was first apparent, areas suitable for grafting were obtained in from fourteen to twenty five days.

This large number of closures performed in one general hospital during thirty five months overseas corroborated the statements of the consultants that "the actual bacterial flora of a wound is a much less valuable guide to the safety of closure than is experienced gross inspection", and that "even when virulent pathogenic organisms are enclosed in wounds during a proper closure there is little danger of a serious or fatal result."



Fig 4—Combined closure and graft of a calf wound. The tract of the perforating gun shot wound had been laid open entirely with considerable skin loss at each end. Closure fifth day. photograph fourteenth day.



A



B

Fig 5 A and B—Closure and graft (latter not shown) of a shoulder disarticulation performed six days after receipt of wound and amputation. Healed and ready for evacuation to the Zone of the Interior three weeks later.

The illustrations are amateur photographs obtained all too infrequently. No regular photographic service was available, an omission which was keenly felt by all services. However, these serve as examples of the problems and the principles of solution. Reparative surgery almost always demands positive

knowledge as to the presence or absence of foreign bodies so that large ones can be removed at the time of closure if necessary. If roentgenograms do not accompany the patient they are obtained prior to operation. Figs 10 and 11 constitute a startling example of the importance of this knowledge in the occasional case. This soldier hit in the right lower quadrant of the abdomen while lying in a foxhole in Sicily with German planes overhead was evacuated by boat to North Africa and a laparotomy performed. The torn intestines were sutured successfully but in the press of work no roentgenograms were taken



Fig. 10. The scale
Treated by
cell against
surgery with

immobilization.

He was passed through three other hospitals before arriving at the Twenty first—traveling some 700 miles by various vehicles during the course of about three weeks. On arrival the laparotomy wound was partially broken down but he had a low grade fever but he was eating well and feeling well. A large abscess was found over the left lumbar area and drainage was about to be done surgically when it was noted that there were no accompanying roentgenograms. Since the abscess was on the opposite side from the wound of entrance and since no exit wound was found and there was no note on the chart in



Fig 6 C and D—Same case as Fig 6 A and B about two years later. No further operative procedure. Slight graft pliable and permanent

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Fig 8 A and B—Extensive wound of upper inner thigh which exposed both the sciatic nerve and the femoral vessels. Note visible abductor femoris muscle bridging gap. Treated by rebridgement on the fifth day, closure and skin graft on the ninth day. Abductor held again in rest of muscles by suturing thigh grafting over it and applying pressure dressing with immobilization.

He was passed through three other hospitals before arriving at the Twenty first—traveling some 700 miles by various vehicles during the course of about three weeks. On arrival the laparotomy wound was partially broken down, he had a low grade fever but he was eating well and feeling well. A large abscess was found over the left lumbar area and drainage was about to be done surgically when it was noted that there were no accompanying roentgenograms. Since the abscess was on the opposite side from the wound of entrance and since no exit wound was found and there was no note on the chart in

needed. In France, five knives were ready each morning, two of these being of the Blair Brown type with Marek roller attachment for men inexperienced in the use of the free knife or for very large sheet grafts, and three being the Army supplied Ferris Smith knives with replaceable blades. For 429 grafts performed on the general surgical service the dermatome was used only three times. Indispensable as it is for certain very special cases, for routine work in reparative surgery it is unnecessary, cumbersome and time consuming. Also, with five or six grafts to be accomplished in a morning by different men,



Fig 8

Fig 8—Lay-on grafts tenth postoperative day



Fig 9

Fig 9—Grooving wound of heel partially severing Achilles tendon. Simple lay on graft obtained from same calf

several of these expensive instruments would be necessary, and considerable time would be wasted in cleaning and re-sterilizing them. But perhaps the most important objection of all to the routine use of the dermatome was revealed by the experience with donor areas. These instruments make possible the securing of grafts without learning the complete technique and in at least

regard to a foreign body roentgenograms were made. Needless to say when the views were seen an ordnance officer patient was consulted prior to operation and his advice closely heeded in removing the 20 mm unexploded airplane cannon shell. It lay loosely within the abscess cavity together with a small piece of bone from the spinal column. Recovery was uneventful and the patient carried home his souvenir now "de loused" of its detonator but still full of TNT.



FIG. 7. A and B—Large superficial defect of thigh grafted on the fifth day; the abdomen was the donor area. Graft sutured in place because of difficult situation to provide proper immobilization.

SIMPLE SKIN GRAFTING

This procedure became an integral part of the closure problem and the term "delayed primary closure" should include in its meaning the use of grafts and flaps wherever necessary. Much has been written on the subject of grafting and for present purposes it will suffice to emphasize only its simplicity. During the year in Africa no skin grafting instruments were available. Having anticipated this before departure from the United States from a perusal of the equipment tables a good quality hollow ground bread knife had been purchased for \$3.50. This knife served its purpose admirably for the fifty odd grafts done in Africa which were large enough to warrant it. The illustration of this knife (Fig. 3) is included solely to emphasize the simplicity of the procedure. Later the all round preparation of the thigh and wrapping of the leg and foot shown in the picture was dispensed with as was the suction box. Thereafter draping was confined to but a few inches beyond the area

to the wound, compressible bulk to fit and elastic stockinet serve very well. Just as fine mesh is much superior to the coarse mesh variety, in that adherence to the wound by the growth of granulations into it is lessened, so nylon and rayon materials, as recently reported, will probably be shown to be even better.

Penicillin was used to protect the "take" on very large grafts and for grafts in areas of obvious contamination. Its value cannot be estimated since, in Italy and France the loss of a graft on these ideal recipient sites was too rare an occurrence to provide study.

The aftercare of grafts during war is frequently neglected. Whether the man is returning to duty or being sent to the Zone of the Interior for further surgery or convalescence, the healed area must be watched for sebaceous collections, small abscesses, encrusted granulation points, and dryness. Certainly here there is a use for lubrication of the skin with petrolatum jelly, cold cream, or lanolin. An excellent coverage may be spoiled by carelessness in this regard.

Chemotherapy, local and systemic, has been adequately discussed in many papers and is not included here. From the experiences at this hospital, proper surgery is by far the most important single factor affecting success.

SUMMARY AND CONCLUSIONS

1 The reparative surgery of soft part wounds is discussed based upon experience with 8445 closures and 429 split skin grafts performed in one general hospital during thirty five months in the North African, Italian, and French theaters.

2 Successful delayed primary closure of war wounds depends upon the following principles: skillful initial surgery at the front, prompt evacuation without disturbance or inspection of the wound, simple suture and/or graft in the general hospital, preferably prior to the sixth day, prompt rehabilitation as soon as healing warrants it.

3 Sound surgical principles are stressed. The skill and judgment of the individual surgeon, not the particular technique used, are the main determinants of success.

4 Petrolatum gauze next to open wounds has definite disadvantages.

5 Dry fine mesh gauze next to the wound and stockinet compression bandages on the outside are the most simple, economical, and effective dressings for closures, grafts and burns under war conditions.

6 Local chemotherapy in closures has not been shown to be significantly useful.

7 Split skin grafts are an integral part of early wound closure, simplicity of technique is stressed.

six patients coming from other hospitals where they had been used the donor area having been denuded too enthusiastically of skin had to be grafted later. No attention had been paid to marked variations in the thickness of the hides of different individuals to say nothing of the variations from inner to outer thigh to calf abdomen back or arm. All donor areas should be healed within two weeks and when properly handled several successive crops of skin may be obtained from the same area. Again it was found that dry fine mesh gauze gave entirely satisfactory results as a donor area dressing the dressing remaining in place until complete healing had taken place. Discomfort on ambulation in the absence of infection or a poorly applied dressing was not increased.



Fig 10



Fig 11

Fig 10—X ray view of German 20 mm aircraft cannon shell (unexploded) lying in scapular cavity of left back. Its presence was unsuspected for three weeks (see text).
Fig 11—Same case as Fig 10 removal of shell.

Methods of applying and fixing grafts in place have been numerous. Many of these for war purposes are unnecessary. The four or five day old wound as yet ungranulating provides an excellent base for a split graft. It is dry and without edema. In most cases the graft can be carefully spread over the area and maintained for several minutes in a state of moderate tension. The normal serum fibrin and thrombin released from both the graft and the recipient area provide their own satisfactory glue to maintain this tension eliminating altogether the necessity for sutures. Fig. 8 is an example of this type. In extensive areas every small tag of skin cut by the knife is made use of by this lay on technique. This is not possible when suturing is depended upon. In other areas a few interrupted sutures or a running stitch serve better especially where the application of a proper dressing is difficult (Fig. 7 A and B). As in all grafting the dressing is all important. It must provide almost complete immobilization of the graft evenly distributed pressure and in incomplete coverages facilities for the escape of serum. Sponges, casts, and mechanics waste are not necessary in most cases. Dry fine mesh gauze next

for use during the second period. Samples were taken from each basin for culture and a comparison of the bacterial counts from the first and last basins afforded an index of the influence of the antiseptic on the number of bacteria remaining on the hands. This technique is based on the assumption that the number of bacteria removed in any given time is proportional to the number on the hands at the time of the scrub (Pohle and Stuart¹).

Technical details were as follows. All materials used were sterilized by autoclaving at 18 pounds' pressure for twenty minutes, the basins, towels and graduates having been wrapped in a double thickness of muslin. The subjects used were all medical students and were carefully instructed in the scrubbing technique. Distilled water 500 cc. was placed in a basin and the subject wet his hands and received 0.5 Gm. Ivory Snow poured onto the palm. The palms and backs of the hands were scrubbed with a sterile brush for five seconds each, then the forearms for fifteen seconds, timed by a stop watch. This procedure was continued with double the time intervals, a fresh supply of Ivory Snow being supplied at the beginning of each minute until a total of five minutes had elapsed. At the end of this period the hands and arms were rinsed with an additional 500 cc. of water and the subject dried his hands with a sterile towel. Then 1 cc. of the wash water was transferred by a sterile pipette to 9 cc. of Beef heart broth* which was shaken rapidly fifty times, and 1 cc. transferred to 9 to 10 cc. of melted agar† at a temperature of about 45° C. The agar was immediately poured into a Petri dish and carefully mixed by gentle agitation before hardening occurred. The bacteriologic procedures were carried out with a minimum of delay, with equal manipulation in all cases and always in duplicate. After forty-eight hours incubation at 37° C. the colonies were counted in a Quebec counter. An identical procedure was carried out on each batch of washings. When the G 11 soap solution was employed during the second scrub period the washings contained a total of about 200 mg. of G 11. This afforded a final dilution of 1:500,000 of G 11 in the agar plate, but the organisms were temporarily exposed to concentrations of the antiseptic varying from 1:50 when the solution was poured into the palm through 1:2,500 and 1:5,000 before and after rinsing to 1:50,000 and finally 1:500,000 in the broth and agar respectively. The final basin provided an estimation of the skin population subsequent to the use of G 11 soap but without the carrying over of significant amounts of the G 11 itself.

In this first series eleven individuals were employed and a total of thirty-eight scrubs were carried out, nineteen with G 11 and nineteen with the neutral liquid soap.

RESULTS

The maximum, minimum and average bacterial counts of washings obtained at the five minute intervals are plotted in Fig. 1. It is noted that the average

*Beef heart broth. 1 pound of beef heart was placed in 1,000 cc. of water in which it was allowed to soak overnight and in the morning was boiled and filtered. To each liter of this broth was added 10 Gm. neopeptone and 10 Gm. NaCl after which the pH was adjusted to 7.3 to 7.4.

†Beef heart agar. To 1 liter of the beef heart broth was added 15 Gm. agar and the pH adjusted to 7.3 to 7.4.

2,2' DIHYDROXY-3,5,6 3',5',6' HEXACHLORODIPHENYLMETHANE
(G-11) AS AN ANTISEPTIC FOR USE IN SURGICAL SCRUBBING

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THE wide variety of antiseptics used for the preoperative preparation of the skin of the surgical patient and the hands of the operator points to the lack of clear cut superiority of any preparation so far introduced. Many of these commonly used have been evaluated by Price,^{1,2} who described a method of study which involved an estimation of the influence of the antiseptic upon the disappearance curve of the skin flora during a cycle of surgical scrubbing. This method was used in a modified form by Hatfield and Lockwood in their investigation of still other skin antiseptics.³ Both reports showed that none of the antiseptics studied had any advantage over 95 or 70 per cent ethyl alcohol as far as the primary reduction of skin flora is concerned. Further related work was carried out, using modifications of the Price technique by Poble and Stuart, with rosin soaps,^{4,5} and by Pillsbury and his co-workers with antiseptics in ointment bases.⁶

This paper offers an evaluation of 2,2' dihydroxy 3,5,6 3',5',6' hexachloro diphenylmethane in a liquid soap base as an antiseptic detergent for a surgical scrub. This compound, hereafter referred to by the manufacturer's code name of G 11, has already been extensively studied by Traub Newhall and Fuller,^{7,8} who have shown that the continued use of a toilet soap containing 2 per cent G 11 has a marked effect on the number of 'resident' bacteria present on the skin. They also showed that G 11 was nonirritating and nonsensitizing as evidenced by some 400 patch tests which were repeated on the same subjects after an interval of from ten to fourteen days. The present paper describes the results obtained by adding 2 per cent G 11 to a standard neutral liquid soap of a type widely used in surgical scrubbing.

MATERIALS AND METHODS

These experiments were carried out by a further simplification of the Price method as modified by Hatfield and Lockwood.³ In the initial series of experiments the scrubbing procedure was divided into three five minute periods with the washings from each period being collected in a separate basin. Neutral Ivory Snow was used during the first and third scrubbing periods. Control experiments were performed with neutral liquid soap during the second period and results compared with experiments in which G 11 was added to this vehicle.

Read (by title) at the meeting of the Society of University Surgeons Boston Mass Feb 12 15 1947

soap
only

growth That part of this effect was due to the carrying over of G 11 antiseptic with the cultures as evidenced by the fact that the final counts, following an additional five minute scrub with Ivory Snow, were substantially higher than those obtained during the antiseptic period The average of final counts was 2,557 per cubic centimeter for the control series and 1,795 per cubic centimeter for the G 11 group, a difference which is scarcely significant Therefore, the action of the G 11 in this series of experiments was principally that of a powerful bacteriostatic agent—a final concentration of only 1 500,000 in the agar plates yielding sterile plates in 60 per cent of the cases After the G 11 had been thoroughly removed by scrubbing with neutral soap, it became apparent that the actual numbers of bacteria on the skin had not been substantially reduced through five minutes of contact with the antiseptic This is consistent with the finding by Traub, Newhall, and Fuller² that the full effectiveness of G 11 can be obtained only by habitual day to day use of G 11 soap

SECOND SERIES

In spite of the lack of evidence of a significant bactericidal action of G 11 on skin bacteria, it was decided to study the effect of its bacteriostatic action on the skin bacteria. The results of this study showed that the wearing of rubber gloves, which is a common practice in the operating room, is highly conducive to proliferation of bacteria on the skin of the hands, that within even one hour of donning gloves, the population of skin bacteria may increase very substantially, and that the consequences of a break in the integrity of a glove increase geometrically in severity with each hour the glove has been worn Therefore, a second series of experiments was carried out, in which operating room conditions were duplicated as closely as possible, consistent with observance of proper conditions for bacteriologic study In view of the findings in the first series it seemed necessary to make certain that no G 11 was present in material used for cultures Therefore, periods of scrubbing with G 11 soap were followed by thorough scrubbing with neutral soap before samples for culture were taken

A total of thirty two scrubs was completed, sixteen with G 11 and sixteen as control with neutral liquid soap

METHOD

The subjects scrubbed under running water for four minutes, divided into ten seconds each for the nails, palms, and backs of the hands, and thirty seconds for the forearms, repeated for each arm and using neutral or G 11 soap as required from a sterile basin At the end of this four minutes each subject scrubbed into 500 cc of sterile water, using 10 Gm Ivory Snow, for thirty seconds on each hand and arm At the end of this period the arms were rinsed with a further 500 cc sterile water, and the subject returned to the sink to repeat the cycle Samples for pour plate counts were taken from the scrub water used during the fifth and tenth minutes When these two cycles were completed, the subjects scrubbed under running water for a further minute to replace a little of the test soap solution onto the hands, dried the hands on

bacterial counts of washings from the first five minute period when Ivory Snow was used, were about 10,000 colonies per cubic centimeter. After five minutes of further scrubbing with neutral liquid soap, the washings averaged about 5000 per cubic centimeter, as contrasted with only 175 per cubic centimeter when 2 per cent G 11 was added to the soap. Furthermore, the lowest count in the neutral soap wash water was 360 per cubic centimeter (in a subject who showed a very low count in the primary washings), while on eleven of the eighteen occasions when G 11 was used, the pour plates showed no

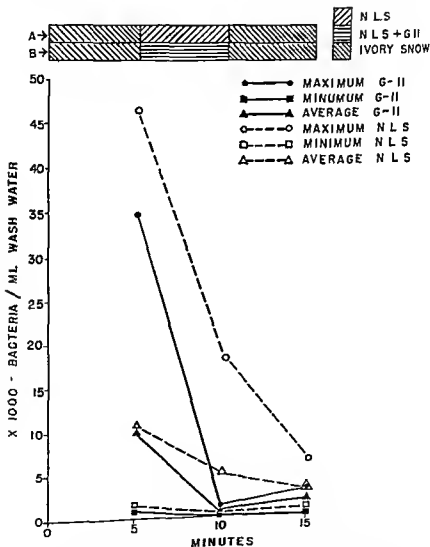


Fig 1—The effect of G 11 in neutral liquid soap (NLS) on bacterial content of wash water during surgical scrubs. The scales A and B refer respectively to the NLS and G 11 scrubs.

adhesive tape After a lapse of one hour, during which the subjects pursued their normal activities, the gloves were carefully removed, avoiding contamination, and the subjects scrubbed only the hands for one minute in 500 cc of sterile water with 10 Gm Ivory Snow, allowing thirty seconds, divided equally, to the nails, palm, and back of each hand Finally, the hands were rinsed with 500 cc of water and the entire contents of the basin were thoroughly mixed The wash water was diluted and plated immediately, as described for the initial series of experiments It should be noted that the wash water used for bacterial counts contained only 10 Gm of Ivory Snow in a liter of water, and that no G 11 was permitted to enter the culture and exercise a bacteriostatic effect

RESULTS

This series of studies indicates that a 2 per cent solution of G 11 in neutral liquid soap exerts a definite antiseptic action on the skin when used in a surgical scrub Fig 2 shows that the bacterial counts on subjects who had used G 11 for two four minute intervals averaged about one third of those on subjects using plain liquid soap under conditions where the possibility of bacteriostatic action of G 11 had been excluded At the end of the hour of wearing gloves, however, the results were even more striking since the counts on the G 11 subjects had further decreased to an average of about 50 per cent of that at the start of the hour while the counts from the control subjects had in the average, almost doubled These data indicate that the number of viable bacteria on the gloved hands increases rapidly when neutral soap is used, but that the number tends to fall during an hour of wearing gloves after a scrub with G 11 soap Traub, Newhall, and Fuller³ stated that G 11 antiseptic soaps, to be effective for surgical purposes, must be used every time the surgeon washes his hands It is our impression that this is not necessarily the case, although it is probably true that the habitual use of G 11 soap is a good method of maintaining the skin flora at a continuously low level

There was no evidence of skin irritation from G 11 in any of twenty subjects who used it repeatedly

SUMMARY

This paper represents an investigation of the effect of a 2 per cent solution of 2,2' dihydroxy-3,5,6,3',5',6' hexachlorodiphenylmethane in a neutral liquid soap It is found that

- 1 When used for a period of five minutes, the G 11 solution left an average of about 70 per cent of the number of bacteria remaining on the hands and arms when the soap vehicle alone was used This was observed in a total of nineteen scrubs controlled by nineteen in which only the soap vehicle was used
- 2 G 11 exercises a marked bacteriostatic effect, even in high dilution
- 3 When used in a series of sixteen ten minute scrubs, controlled by sixteen ten minute scrubs with plain neutral soap, the G 11 soap left on the skin an average of about one third as many bacteria as occurred when neutral liquid soap was employed under identical conditions When the subjects wore surgical

a sterile towel, and donned surgical gloves with aseptic precautions. This last one minute period was employed in order to demonstrate any persistent effect of the G II solution since it was felt that after the basin scrub with the Ivory Snow there would be an insufficient quantity of the G II left on the skin to exert any appreciable continuing bacteriostatic effect. In order to provide full encouragement to bacterial growth, 2 cc of the beef heart broth were then poured into the gloves and the wrists sealed off with gauze bandages and

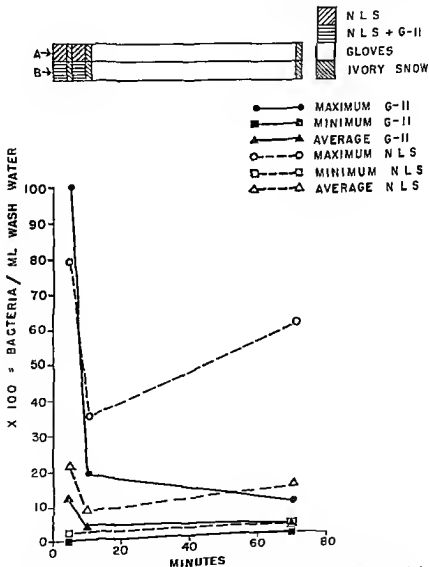


Fig. 2.—The influence of G II in neutral liquid soap (NLS) on bacterial flora of skin during subsequent wearing of surgical gloves. The scales A and B at the top show the time intervals for the NLS and G II scrubs respectively.

A METHOD OF STATISTICAL ANALYSIS

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ANYONE who has ever endeavored to report the long term end results in a series of cases must have been impressed at some stage of the study with the inherent difficulties of being accurate. He finds that the number of cases in his series increases each year, that old cases are lost each year, and that people die each year, due either to the disease in question or to other causes. By the time he has charted the information on the first twenty five cases it has probably become apparent to him that it is going to be difficult to express the end results in the form of one easily comprehensible figure. Unless he is experienced at handling the problem, he will probably start all over again, defining the criteria regarding length of follow up, etc., that each case must satisfy, and, after one or more false starts and considerable floundering, will end up with an analysis with which he will be satisfied and a set of figures which may or may not be statistically valid. The extent to which such inaccuracies concern medical authors can best be judged by reading the literature, which is full of loose statements regarding end results.

In a study of the end results of gastroenterostomy in the treatment of peptic ulcer we became impressed with the inherent difficulties in the problem of reporting. It became apparent that there was great need for a system of recording, summarizing and presenting clinical material that would give the reader a clear, accurate picture of long term results.

To illustrate the problems and the need for a system, the end results in peptic ulcer treated by posterior gastroenterostomy are reported, using the various methods commonly encountered in the medical literature. The defects and limitations of each of these methods are commented upon. Finally, a method of analyzing and reporting is developed which avoids many, if not all, of the faults of the more popular systems, and gives, we believe, an accurate graphic picture of the long term results of posterior gastroenterostomy.

This method can be used in an analysis of any group of cases, and the curves obtained offer a clear method for comparing two groups of cases. The advantages of the method are (1) every case in a series can be utilized, there is no selection of material in a series, (2) it allows for comparison of two series of cases, even though the series differ in size and length of follow-up period (3) it may be graphic which facilitates comprehension by the reader, (4) it is believed that the method is statistically sound and that it gives a true picture of the accumulated experience.

Clinical Material—The clinical material includes all the posterior gastroenterostomies done for peptic ulcer at the New York Hospital between Oct. 1,

Study done under a Lewis Cass Ledyard, Jr. Fellowship

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gloves containing nutrient broth for sixty minutes after the scrub, the subjects who had used G 11 soap showed a decrease in the number of skin bacteria to about 50 per cent of the count at the beginning of the hour, while the control subjects showed an increase of about 100 per cent over the population present when the gloves were applied

4 The addition of 2 per cent of this antiseptic to liquid surgical soap results in a substantial enhancement of the efficiency of the soap in reducing the possibility of wound contamination following puncture or tearing of a glove but only if the residual G 11 is not washed from the hands before the gloves are applied

5 No evidence of skin irritation was observed following repeated use of soap containing 2 per cent G 11 by twenty subjects

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 Used in Soap Further Practical Studies Arch Dermat & Syph 52 390 1945

Comment—While this statement is perfectly accurate it is so loose that it may have inaccurate implications. One series of cases so reported might have a high proportion of cases with long follow up and another might consist largely of cases with a short follow up. Only 2 cases in this series of 264 cases were actually followed fourteen years after operation. Using this broad method gives the best possible percentage of end results. Certainly the method is not sufficiently accurate to compare two ways of treating peptic ulcer unless the two groups were found to be comparable in duration of follow up a situation that seldom maintains in two series of cases.

Method 2—A second method commonly used is to exclude cases that were lost or patients who died during the first year after operation and base the end result study on the remaining group of cases. If we do this we find that 261 out of 264 cases were followed one or more years. The poor results remain the same (48 cases) and we can make the following statement: *In 251 cases followed one to fourteen years the satisfactory results are 80.9 per cent the unsatisfactory results 19.1 per cent.*

Comment—This method is open to the same criticism as Method 1. It will be noted however that this effort at greater accuracy has increased the poor results about 1 per cent.

Method 3—Another common method of reporting involves the use of an average follow up period for the group of cases. Thus if we compute the average follow up period for the 264 operative survivors it is found to be 6.2 years. We might state therefore: *In 264 operative survivors with an average follow up period of 6.2 years there have been 18 recurrences or 18.2 per cent.*

Comment—The implication is that 264 cases have been followed 6.2 years which is not true. Further it is a poor method for comparing two groups of cases even if they have the same average follow up period because one group might be weighted with cases followed one year and another with cases followed fourteen years. For these reasons the method cannot be recommended for comparing two groups of cases.

Method 4—In this method the cases of a series are grouped into follow up periods that is cases followed three or more years, five or more years, ten or more years, etc. If we do this for our group of 264 operative survivors then list the poor results occurring in each group we can report as follows: *In the group of 264 operative survivors 201 were followed three or more years with 39 poor results or 19.1 per cent, 155 were followed five or more years with 34 poor results or 22 per cent, and 66 were followed ten or more years with 15 poor results or 22.7 per cent.*

Comment—This statement is perfectly accurate both in fact and in implication and the method is a very good one. If for instance the percentages of poor results in the groups followed three, five, and ten years are compared with the failure curve at the three, five, and ten year levels (see Fig. 2) it will be observed that the figures practically coincide. In carrying out this method however poor results not followed three, five, and ten years must be discarded from their respective groups. If this were not done in this instance the per-

TABLE I LIST OF POSTERIOR GASTROENTEROSTOMIES BY CALENDAR YEAR SHOWING OPERATIVE DEATHS AND SURVIVORS

COLUMN 1	COLUMN 2	COLUMN 3	COLUMN 4	COLUMN 5
YEAR OF OPERATION	NUMBER OF OPERATIONS	OPERATIVE DEATHS	OPERATIVE SURVIVALS	CUMULATIVE OPERATIVE SURVIVALS
1932	3	0	3	3
1933	22	2	20	23
1934	35	0	35	58
1935	24	3	21	79
1936	25	2	23	102
1937	25	0	25	127
1938	24	1	23	150
1939	19	0	19	169
1940	16	0	16	185
1941	11	0	11	196
1942	16	1	15	211
1943	30	0	30	241
1944	13	0	13	254
1945	10	0	10	264
Totals	273	9 (3.3%)	264 (96.7%)	

1932, and Dec 31, 1945, and is shown in Table I, which lists the number of posterior gastroenterostomies done in each calendar year (Column 2), the operative deaths each calendar year (Column 3), the number of operative survivors each calendar year (Column 4), and the cumulative operative survivors at each calendar year level (Column 5). Thus, by the end of 1945, we see that 273 posterior gastroenterostomies had been done for peptic ulcer, with nine operative deaths (an operative mortality of 3.3 per cent). The 264 cumulative operative survivors form the basic group that could be followed and upon which statements regarding long term results could be made. Discussion later in this paper will illustrate how this group is modified by deaths occurring during the years of follow up.

The individual patients surviving operation are studied, and the poor results are listed. In so doing, we discovered that there are 48 cases with poor results. A poor result, of course must be clearly defined. In this study, any result is considered poor if the patient (1) has to be rehospitalized for peptic ulcer in this or any other hospital or (2) has any evidence, either by history or examination of bleeding from the upper gastrointestinal tract or (3) has either clinical or x ray evidence of a marginal ulcer. This includes all patients requiring reoperation and all patients having many gastric complaints after gastroenterostomy. It does not include a number of patients with pain, gas, belching, or indigestion, all of a mild or transient nature. These cases are considered satisfactory results.

Method 1—The first method considered is the one most frequently used for reporting cases in the medical literature. The cumulative operative survivors (264 from Table I, Column 5) are divided into the poor results occurring during the fourteen year period of study (48 cases), and the following statement is made: *In 264 patients operated upon one to fourteen years ago, the poor results total 48 cases, or 18.2 per cent, the satisfactory results, 81.8 per cent*

The method that is worked out and presented in this paper makes use of every case in the series and every year that the case is followed. The cases are grouped in follow up years irrespective of operative year and the poor results occurring in each follow up year are determined. This gives us two figures poor results and cases followed for each year after operation. These are converted to percentages and recorded as accumulating percentage giving a curve which represents the entire experience for each year of follow up. A detailed description of the method follows.

The cases in the series are recorded first as in Table I (previously described) giving the cumulative operative survivors by calendar year (Column 5). These same cases are then arranged by follow up years by charting them in Table II. Each operative survivor is charted under the year last seen or in case of death under the year of death. The number of cases charted under each horizontal year in Table II must equal the number of operative survivors that year (from Table I Column 4). By adding the cases diagonally one gets the number of cases followed in each follow up year. These are charted in Table II Column 1. Since any case followed fourteen years is also followed thirteen years, the cases are accumulated as in Table II Column 2. Table II Column 2 gives the number of cases actually followed each follow up year from zero to fourteen years irrespective of calendar year of operation.

The 48 poor results or failures of posterior gastroenterostomy are recorded in Table III under the calendar year in which the case in question first became

TABLE III DISTRIBUTION OF POOR RESULTS IN FOLLOW UP YEARS

CALENDAR YEAR		FOLLOW UP YEARS														COLUMN 1		COLUMN 2	COLUMN 3	COLUMN 4	F U YEAR
OPERATIVE	FOLLOWED	32	31	34	35	36	37	38	39	40	41	42	43	44	45	46	POOR RESULTS IN F-U YEAR	COL. 1 COL. 2 TABLE II	PERCENT AGES IN F U YEAR	CUMULATIVE PERCENT AGES	
1932				1	2												0	$\frac{0}{2}$	0	25.2	14
1933					2	3	1	2	4								0	$\frac{0}{5}$	0	25.2	13
1934				1	3	1	4	2	6								1	$\frac{1}{31}$	3.2	25.2	12
1935						3	1	5	1	6							0	$\frac{0}{50}$	0	22.0	11
1936									1	3	4						0	$\frac{0}{60}$	0	22.0	10
1937										2	4						0	$\frac{0}{80}$	0	22.0	9
1938									3	1	2		1				0	$\frac{0}{100}$	0	22.0	8
1939											1		1				2	$\frac{2}{122}$	0.8	22.0	7
1940												3	4				0	$\frac{0}{141}$	0	21.2	6
1941														1			4	$\frac{4}{155}$	2.6	21.2	5
1942																	7	$\frac{7}{173}$	4.0	18.6	4
1943																		$\frac{4}{204}$	2.0	16.6	3
1944														3	2	1	4	$\frac{10}{232}$	4.3	12.6	2
1945															2		17	$\frac{17}{251}$	6.8	8.3	1
1946																	4	$\frac{4}{255}$	1.6	1.5	0

† Poor result that has subsequently become a good result on conservative treatment.

Failure Curve for 100 Cases—In an effort to test the accuracy of the failure curve, the first 100 cases of gastroenterostomy that had been followed eight years were analyzed by the same method. For each follow up year from one to eight we had the same 100 cases. All cases that were not followed eight years were discarded. The poor results were determined in this standard sample of 100 cases and recorded in the year in which the case first became a poor result. The failure curve for these 100 cases is recorded in the broken line in Fig. 1. It will be noted that the two curves coincide reasonably well. This supports the view that the failure curve is an accurate method for expressing end results.

TABLE IV METHOD OF MODIFYING THE FAILURE CURVE

COLUMN 1	COLUMN 2	COLUMN 3	COLUMN 4	COLUMN 5	COLUMN 6	COLUMN 7	COLUMN 8
FOLLOW UP YEAR	POOR RESULTS	CUMULATIVE POOR RESULTS	"G" CASES	CUMULATIVE "G" CASES	NET POOR RESULTS	PER CENT ON FAILURE CURVE	PER CENT ON MODIFIED FAILURE CURVE
1	21	21	1	1	20	8.4	8.0
2	10	31	2	3	28	12.7	11.5
3	4	35	4	7	28	14.7	11.8
4	7	42	2	9	33	18.7	11.7
5	4	46	3	12	34	21.3	15.7
6	6	46	0	12	34	21.3	15.7
7	1	47	1	13	34	22.1	16.0
8	0	47	1	14	31	22.1	15.5
9	0	47	0	14	33	22.1	15.5
10	0	47	0	14	33	22.1	15.5
11	0	47	0	14	33	22.1	15.5
12	1	48	0	14	34	25.3	17.9
13	0	48	0	14	34	25.3	17.9
14	0	48	0	14	34	25.3	17.9

Method of Changing the Failure Curve—In certain clinical groups, particularly peptic ulcers, an author may wonder what to do with the case that is a poor result in one follow up year and a good result in later follow up years. One can argue that this case should not be recorded as a poor result yet it must be so considered according to the original definition. If we wish to modify the poor results by those that later become good results due to conservative treatment, we go through the following maneuver. Every poor result that becomes good is designated as "g" on Table III under the year in which it finally becomes good. The "g's" are then added obliquely, and the figures recorded in Table IV. Column 4. Table IV shows the follow up year in Column 1, the number of poor results in each follow up year in Column 2 (from Table III, Column 1), the cumulative poor results at each year level in Column 3, the poor results that become good in Column 4, the cumulative poor results that become good in Column 5, the net poor results in Column 6 (Column 3 minus Column 5), the percentage of poor results at the level of each follow up year (from Table III, Column 4) in Column 7 and the percentage of net poor results in Column 8. If these percentages are recorded they give us the failure curve after conservative treatment which is shown in the broken line in Fig. 2. The solid line in Fig. 2 is the failure curve recorded in Fig. 1.

a poor result. The marginal ulcers are recorded under the year in which the symptoms of marginal ulcer first appeared rather than under the year of operation for marginal ulcer. By adding these cases diagonally we get the number of poor results in each follow up year. These are recorded in Table III, Column 1. In Table III, Column 2 the fraction showing poor results over cases followed is recorded, the denominator being taken from Table II, Column 2. In Table III, Column 3, each fraction is converted to per cent, which is the ratio between poor results and cases followed each follow up year. In Table III, Column 4 these percentages are added. They are plotted in Fig 1, which is called the failure curve. It will be noted that the poor results of gastroenterostomy measured in this way come to 25.2 per cent at the fourteenth year.

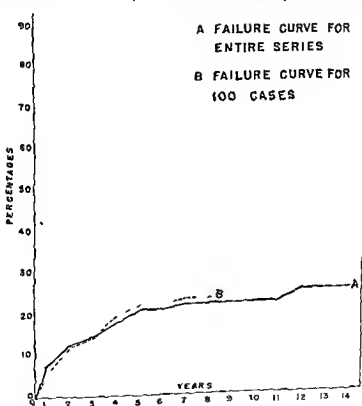


Fig 1—Failure curve

Comment on the Method—From the foregoing analysis it must be clear to the reader that the only accurate way of measuring end results is on a year to year basis determining for each follow up year the number of poor results in relation to the number of cases actually followed. The various maneuvers may appear complicated, but are really quite simple. If the method described is carefully followed, the analyst will get the significant figures out easily and quickly.

of any operative procedure is death due to the operation. If we wish to take operative deaths into account in the failure curve, it can be done by charting the percentage of operative mortality for the entire series (3.3 per cent) across the bottom of the graph, and superimposing the failure curve on this by starting at 3.3 per cent instead of 0 per cent. This is illustrated in Fig 3, which shows the operative mortality, the failure curve charted on top of it, the failure curve modified by those cases which became good results after conservative treatment, and the failure curve modified by those cases which became good results after both conservative and further operative treatment. (The figures for this last curve are not included in this paper.) Herein we have a graphic method of presenting a considerable mass of complicated yet related information which is much easier for the reader to comprehend quickly than the tables on which the graphs are based. The basic tables should always be

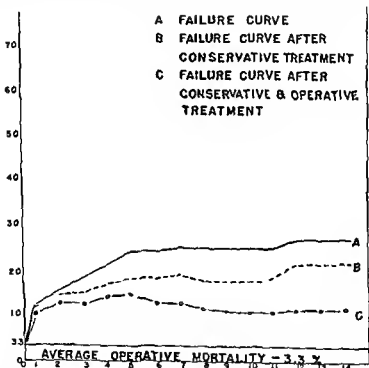


Fig 3—Failure curve modified by operative mortality and by good results after conservative and operative treatment

given to enable the reader who may be particularly interested to check back on the size of the series presented and the number of cases that have been followed each year.

Completeness of Follow up and Its Significance—In any discussion among doctors concerning end results someone invariably asks what to do with the lost cases. There is only one answer to this question: *Lost cases cannot be con-*

The formula for obtaining the percentages in the failure curve after conservative treatment follows. The percentage must be calculated for each follow up year, and the figures are all taken from Table IV.

Column 3 Column 6 Column 7 Column 8 or

Cumulative poor results net poor results failure curve % modified curve %
For the first follow up year this is 21 20 8.4% $\frac{20}{24}$ equals 80%

It is necessary to calculate any modifications of the failure curve in this manner. If we should attempt to compute the modified failure curve in the same way the original failure curve was calculated (as in Table III), we would find the modified curve greatly distorted. This is because cases originally recorded as poor become good in later follow up years. Since the denominator is smaller for each succeeding follow up year (Table III, Column 2), we would find that if all our cases became good results we would end up below the 0 per cent line, unless we follow this formula.

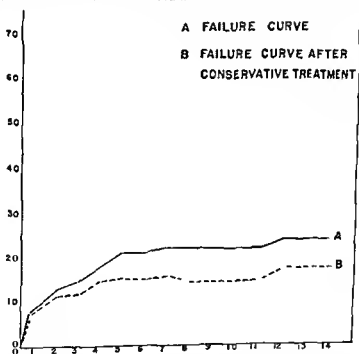


Fig. 2—Failure curve modified by good results after conservative treatment.

The failure curve can be modified in any way desirable. If we should like to know our net poor results after further surgery, we could chart these cases in Table III, tabulate the figures and compute and plot another modification of the failure curve. This is done in Fig. 3 but for the sake of simplicity the figures are omitted.

Operative Mortality in the Failure Curve—Another useful modification of the failure curve concerns operative mortality. In a sense the first failure

considered in follow up studies Philosophers may say that a high proportion of the lost cases are good results, or are bad results, but, in the end, whatever anyone says regarding unfollowed cases remains philosophy. Many factors influence the ratio of good to poor results in the lost cases. Not the least of these is whether the patient has gone to the institution of his own choosing, and whether the institution enjoys a fine reputation with the public. There is some support for the view that the ratio of good to poor results is the same in the lost as in the followed group in the New York Hospital, yet this view must remain in the realm of opinion rather than fact.

Consideration of the follow up is important in any study of end results because it tells the reader the extent to which the followed cases might be selected cases, or how much of the total picture the author has been able to observe and to report. For instance, at the first follow up year level our experience is 97 per cent complete (251 out of 259 cases), and by the sixth follow up year it has become 85 per cent complete (141 out of 166 cases). In another series of cases we might find that our experience was but 50 per cent complete by the sixth year. We could not know with certainty, therefore, that the end results in the two groups were truly comparable. A difference in the end results might be either wiped out or exaggerated if the follow-up were more complete. It is a corollary that in comparing end results in two groups of cases, the completeness of follow up should be reasonably similar. If it is not the two groups may not be comparable, and differences may be artificial rather than real.

As we have observed earlier in this study, average follow up time is of limited significance. The most accurate way of expressing the completeness of follow up of a series is to determine the ratio of lost to followed cases at the level of each follow up year. This is done as follows:

The cumulative operative survivors (from Table I, Column 5) is the basic group that could be followed, but must be corrected for deaths that occur from time to time during the follow up period, due either to ulcer or to other diseases. To correct for deaths, the patients in the series who die are charted under the calendar year of death and subtracted from each subsequent calendar year that they could be exposed to follow up. This is done in Table V, in which Column 1 shows the cumulative operative survivors (from Table I, Column 5). Column 2 the deaths to be subtracted from them, and Column 3 the cumulative net survivors. Cumulative net survivors is the number of cases that could have been followed at the level of each follow up year if no cases were lost. The ratio between cases actually followed each year (from Table II, Column 2) and cumulative net survivors is charted on Fig. 4 which is called the follow up curve. The percentage above the line is not followed (lost) and that below the line is followed. Thus we see that the efficiency of the follow up decreases from 100 per cent (operative survivors) down to 42 per cent in the thirteenth year (8 out of 19 cases), but in the fourteenth year it goes up to 100 per cent. The two patients operated upon fourteen years ago who lived fourteen years have been followed all the way through

TABLE 1. DISTRIBUTION OF DEATHS OCCURRING IN THE FOLLOW UP YEARS

[illegible]

sidered in follow up studies Philosophers may say that a high proportion of the lost cases are good results or are bad results, but in the end, whatever any one says regarding unfollowed cases remains philosophy. Many factors influence the ratio of good to poor results in the lost cases. Not the least of these is whether the patient has gone to the institution of his own choosing and whether the institution enjoys a fine reputation with the public. There is some support for the view that the ratio of good to poor results is the same in the lost as in the followed group in the New York Hospital yet this view must remain in the realm of opinion rather than fact.

Consideration of the follow up is important in any study of end results because it tells the reader the extent to which the followed cases might be selected cases or how much of the total picture the author has been able to observe and to report. For instance at the first follow up year level our experience is 97 per cent complete (251 out of 259 cases) and by the sixth follow up year it has become 85 per cent complete (141 out of 166 cases). In another series of cases we might find that our experience was but 50 per cent complete by the sixth year. We could not know with certainty therefore that the end results in the two groups were truly comparable. A difference in the end results might be either wiped out or exaggerated if the follow up were more complete. It is a corollary that *in comparing end results in two groups of cases the completeness of follow up should be reasonably similar*. If it is not the two groups may not be comparable and differences may be artificial rather than real.

As we have observed earlier in this study average follow up time is of limited significance. The most accurate way of expressing the completeness of follow up of a series is to determine the ratio of lost to followed cases at the level of each follow up year. This is done as follows.

The *cumulative operative survivors* (from Table I Column 5) is the basic group that could be followed but must be corrected for deaths that occur from time to time during the follow up period due either to ulcer or to other diseases. To correct for deaths the patients in the series who die are charted under the calendar year of death and subtracted from each subsequent calendar year that they could be exposed to follow up. This is done in Table V in which Column 1 shows the cumulative operative survivors (from Table I Column 5), Column 2 the deaths to be subtracted from them and Column 3 the cumulative net survivors. *Cumulative net survivors is the number of cases that could have been followed at the level of each follow up year if no cases were lost*. The ratio between cases actually followed each year (from Table II Column 2) and cumulative net survivors is charted on Fig. 4 which is called the follow up curve. The percentage above the line is not followed (lost) and that below the line is followed. Thus we see that the efficiency of the follow up decreases from 100 per cent (operative survivors) down to 42 per cent in the thirteenth year (8 out of 19 cases) but in the fourteenth year it goes up to 100 per cent. The two patients operated upon fourteen years ago who lived fourteen years have been followed all the way through

Other Methods Presented in the Literature—In 1943 Hollander and Mage* presented a statistical method for evaluating the results of treatment for peptic ulcer. Their paper is a contribution to the problem, yet we cannot endorse their method as being statistically sound and accurate. After some preliminary logic they stated: "We believe that the incidence of failure among this group of patients (the lost or not followed group) is no greater than among

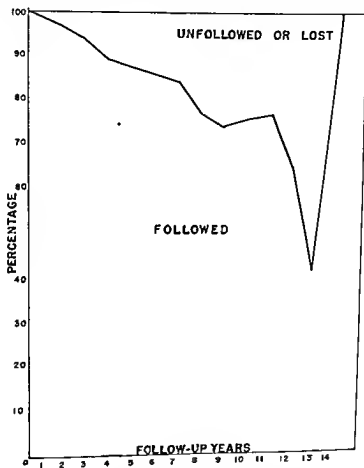


Fig. 4—Follow up curve

those who return to follow up year after year (the observed group), and it may even be less." They then proceed to develop a statistical method of analysis based upon maximum and minimum percentages of failures for each follow up year. If the quoted premise is true, there is no need for a maximum and minimum, for the results in the lost cases would coincide with those in the followed cases. But if it is not true, the maximum and minimum curves should certainly not be as they describe them. Logically, the maximum curve

*Hollander F and Mage G. *Surg. Gynec. & Obst.* 78: 523-546, 1943

should consider all of the lost cases as poor results, and the minimum, all lost cases as good results. If this logic is pursued in the clinical material presented herein, the failure curve is absurdly high and loses all significance. Further, these authors fail to correct their operative survivors for deaths that occur during the follow up period. We can subscribe to their general idea of a cumulative failure curve, and to the concept of an index of failure obtained from this curve. The index of failure however varies in the follow up years. For instance we can state that our index of failure for posterior gastroenterostomy is 21.2 per cent at the fifth follow up year and 22.0 per cent at the tenth follow up year.

Application of Standard Error, and Significant Difference—The primary thesis of this paper is the presentation of a method for recording information. A method has been developed which gives us true a picture as we know of our experience. One may inquire of the figures presented regarding their standard error. Or if by this method we were to compare two groups of cases, one might ask if the difference in the two failure curves is a significant difference. Standard error and significant difference are both vital tools of the statistical method which should be applied to these figures if one is to evaluate, not the method but the figures themselves.

SUMMARY

- 1 A method of analyzing and reporting clinical material has been described which it is believed is accurate and statistically sound*. It is believed that the method can be applied to other groups of clinical cases.
- 2 By this method it is possible to report every case in the series without selection of material within the series.
- 3 The method is graphic which facilitates comprehension by the reader.
- 4 The method is easily adaptable to testing by standard statistical methods.
- 5 The method is compared with other methods that are commonly employed and the defects and limitations of each are commented upon.

For many hours of patient help and criticism the author is greatly indebted to Dr. John W. Fertig of the Columbia University School of Public Health. His facile biostatistical knowledge guided me through many common statistical pitfalls. If the method herein described is sound and widely applicable it is his expert advice that has made it so. If it is not, he is to be exonerated.

*The authors are (1) Poor years, according in subsequent follow up the first year the second year is not 5/100 but 5/50 (2) Percentages cannot be added directly on a graph but should be added according to the formula $1 - (\text{the product of } 100 - \% \text{ failure for each follow up year})$

The first error makes the rate of failure for each year too low because the denominators in Table III Column 2 are too high.

PERIPHERAL EXTENSION OF RADIOPAQUE MEDIA FROM THE SUBARACHNOID SPACE

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(From the Departments of Surgery [Neurosurgery] and Radiology, The University of
Rochester, School of Medicine and Dentistry)

INTERPRETATION of pantopaque myelograms rarely presents difficulties when the examination is properly conducted. Occasionally, an atypical pattern may be obtained as a result of faulty technique or of anatomic abnormality. Peripheral extension of the medium along the spinal nerves is unusual but occurs often enough to justify special consideration. Such peripheral extension has been noted by others^{1,2} using pantopaque or other myelographic media and has been observed in 4 of the first 200 pantopaque myelograms done at Strong Memorial Hospital.

In this paper these four atypical myelograms are discussed in relation to a variety of observations on experimental contrast neurography which have been reported elsewhere.^{3,4} It seems evident that both clinically and experimentally a medium escapes along the peripheral nerves only under distinctly abnormal circumstances. Accordingly, the collective results have little bearing on whether there is a direct communication between the subarachnoid space and the perineural spaces of peripheral nerves. They do, however, show that a connection can be established and this may be significant in relation to local anatomic anomalies, pathologic processes, and injection irregularities.

CLINICAL CASES

Extension of the pantopaque outside the normal confines of the subarachnoid space was encountered in all four cases in the course of routine myelography.

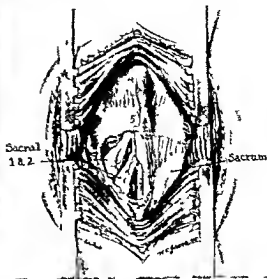
CASE 1 (SMH No. 232661)—Immediately after the medium was injected it was seen fluoroscopically to flow out of the lumbar cistern and to globulate on the left side (Fig. 1, A). These globules disappeared when the patient was tilted head down, suggesting that diverticula were being emptied. When laminectomy was performed for removal of a protruded disc at the fourth lumbar vertebra the reason for the unusual myelogram was clearly demonstrated. The first and second roots were seen to be encased in large diverticular extensions of meninges that contained fluid which could be emptied on compression (Fig. 1 B).

CASE 2 (SMH No. 219084)—Since routine radiographs showed pronounced changes from the second to fourth lumbar vertebrae, consistent with a diagnosis of Charcot spine, lumbar puncture for the injection of pantopaque was made at the fifth lumbar interspace. After injection the medium did not flow as the patient was postured. From the radiograph (Fig. 2) taken after 3 cc of pantopaque had been injected it was evident that the tip of the spinal canal and that the medium lay several nerve roots. The pantopaque injection but was removed without difficulty.

This work was aided by grants from the Department of Surgery, School of Medicine and Dentistry, The University of Rochester and from the Research Laboratories of the Eastman Kodak Co., Rochester, N. Y.
Read (by title) at the meeting of the Society of University Surgeons, Boston, Mass., Feb. 13 to 15, 1947.



A



B

Fig 1—A Myelogram showing the filling of diverticula in Case 1. B Operative exposure showing the anatomic defect visualized in the myelogram.



Fig 2—Myelogram showing the extension of pantopaque for short distances along the nerve roots in Case 2. Complete subarachnoid obstruction is shown at the upper margin of the opaque column. The lumbar puncture needle is placed eccentrically and appears to be lodged in the first sacral nerve root.

tempt was made to aspirate any of the medium. Check radiographs taken at various intervals (Fig 3 B C and D) over a period of five months showed that the medium apparently was fixed in position; that the relative distribution remained the same and that the amount decreased significantly.

CASE 4 (SMH No 33594).—Only a few drops of spinal fluid were obtained at myelography but the medium was injected nevertheless. The distribution that obtained immediately after the injection is shown in Fig 4 A. Under fluoroscopic visualization the medium was seen to flow easily in a cephalad direction but when the lumbosacral region was



Fig 4.—Radiographs taken (A) at the time of the injection of pantopaque and (B) two days later in case 4. The lumbar puncture needle is located in the first sacral nerve root on the right. Some of the medium has entered the subarachnoid space but the remainder has spread into the lumbosacral plexus on the side of injection only.

examined the medium was seen to have escaped along the fifth lumbar and first sacral roots on the right side. These areas appeared fairly broad and irregular in outline. None of the medium could be aspirated at the end of the examination. Radiographs taken two days later visualized the distribution shown in Fig 4 B. Fourteen months later all the medium along the nerve tracts had disappeared and only a small amount—estimated at 0.2 cc—was present at the termination of the lumbar sac.

EXPERIMENTAL STUDIES

Experiments were carried out in rats, rabbits and dogs to study the behavior of radiopaque media in peripheral nerves and in the subarachnoid space. The extension of fluid solutated compounds of varying viscosities was studied.

culty twelve days later by means of a second lumbar puncture. Determination of the spinal fluid protein in the first sample gave a value of 90 mg per cent.

CASE 3 (S.M.H. No. 173025).—Lumbar puncture was performed at the third interspace. 7 cc of spinal fluid were withdrawn and 5 cc of pantopaque injected. On fluoroscopy most of the medium was seen to be distributed along the nerve roots as shown in Fig. 3, A, but a small amount still flowed freely on manipulation of the patient. No at-

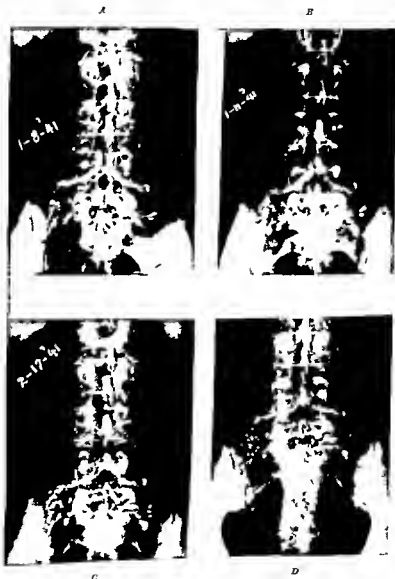


Fig. 3.—R. J. rographs made at various intervals after the injection of pantopaque in Case 3. A, At the time of injection. B, three days later. C, five weeks later, and D, five months later. Only a small amount of the medium is present in the lumbar cistern, the remainder having extended into the peripheral nerves. The relative position of the medium in the nerves has not altered in five months although the amount has diminished considerably. (From Steinhausen, T. B., and others. *Radiology* 43: 231-23, 1944.)

arachnoid space occurred only under considerably greater pressure and in dogs took place when pressures of 165 to 200 mm of Hg were applied. Extravasation of a medium occurred after inaccurate injection on the development of excessive pressure and occasionally when the medium reached a region of plexus formation in the nerve. An example of the extravasation at a plexus is shown in a radiograph (Fig 5) obtained after iodobenzene had been injected in a single fasciculus of a dog nerve. As is shown in the illustration the medium traveled proximally to the nerve plexus where extravasation occurred. From this site the medium extended in two directions under the same injection pressure. A portion continued on into the subarachnoid space and a second column of medium returned in a centrifugal direction in another area of the nerve.



Fig 6—Sections from a rabbit nerve following injection of iodobenzene tinted with printer's ink. A just above site of injection in the peroneal nerve at the knee, and B at level of dorsal root ganglion. The medium is centrally located in the peripheral portion of the nerve but comes to lie in peripheral axonal clefts at the level of the ganglion.

There was never evidence of rapid spontaneous flow of the media in the perineural spaces but in chronic experiments where pantopaque was used a very slow centripetal motion of the medium was evident some weeks after the injection. In passing it may be noted that iodobenzene was very irritating to nerves and produced severe damage whereas pantopaque appeared to be very satisfactory for chronic experiments.

Microscopic sections at various levels of the nerves and roots showed that at the site of injection the carbon tinted media occupied the central portion of the endoneurium. Followed centripetally the injected mass occupied a

both visually and radiographically after injection under measured pressures into the perineural spaces of peripheral nerves and into the subarachnoid space. Many of the experiments were acute, and in these it was frequently desirable to tint the media by the addition of small amounts of printer's ink. In the acute experiments iodobenzene was usually used and in the chronic studies pantopaque was employed.



Fig. 5.—Experimental neurogram in a dog, showing extension of iodobenzene in a single fasciculus to a point of extravasation at the lumbosacral plexus. Following this break through the medium extends both to the subarachnoid space and centrifugally along another portion of the nerve.

Extension of Media Injected Into Peripheral Nerves—After cannulation of a single fasciculus in the common peroneal nerve at the popliteal space an injected medium flowed easily both proximally and distally and remained confined to the perineural spaces (see Fig. 6). The extension was visualized radiographically as a single line or a series of parallel fine lines extending from the point of injection to the subarachnoid space proximally and into the midfoot distally. Some pressure was required for the injection and this varied with both the species and the area of the nerve being traversed by the medium. In the nerves of rats and rabbits pressures of the order of 50 to 80 mm. of Hg were required to cause extension whereas in dogs pressures ranging from 96 to 138 mm. of Hg were necessary. Penetration of the medium into the sub

arachnoid space occurred only under considerably greater pressure, and in dogs took place when pressures of 165 to 200 mm of Hg were applied. Extravasation of a medium occurred after inaccurate injection, on the development of excessive pressure and, occasionally, when the medium reached a region of plexus formation in the nerve. An example of the extravasation at a plexus is shown in a radiograph (Fig 5) obtained after iodobenzene had been injected in a single fasciculus of a dog nerve. As is shown in the illustration the medium traveled proximally to the nerve plexus where extravasation occurred. From this site the medium extended in two directions under the same injection pressure. A portion continued on into the subarachnoid space and a second column of medium returned in a centrifugal direction in another area of the nerve.

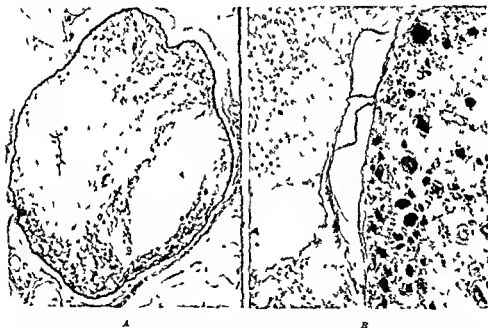


Fig 5—Sections from a rabbit nerve following injection of iodobenzene tinted with printer's ink. A just above site of injection in the peroneal nerve at the knee, and B, at level of dorsal root ganglion. The medium is centrally located in the peripheral portion of the nerve but comes to lie in perineural clefts at the level of the ganglion.

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more peripheral location in the fasciculus until at the lumbar plexus it appeared in clefts on the inner surface of the perineurium or the perineurial septa still confined to a small portion of the total sheath extent. From these clefts the medium escaped into the subdural space and apparently by break through into the subarachnoid space. Subarachnoid entrance always occurred through the perineurium and never in the periaxonal tissues. Sections of rabbit nerves illustrating certain phases of the passage of a medium are shown in Fig 6 A and B.



Fig. —Filling of peripheral nerves of a dog from the "subarachnoid space" by the application of relatively high pressure. The lumbar extremity has been dissected away to show more clearly that the iodobenzene is present in several nerves and the filum terminale.

Behavior of Media Injected Into the Subarachnoid Space—In the course of the development of pantopaque intrathecal injections were made in ninety-four dogs and many of the animals were kept under observation for one year or more. Of this group serial radiographs were made on twenty-three dogs at varying intervals but in no instance was there evidence of the medium extending out of the normal confines of the spinal subarachnoid space along the peripheral nerves. On the other hand there was a smaller group of dogs in which iodobenzene was introduced into the subarachnoid space and in this

group the result was somewhat different. The introduction of iodobenzene was always fatal but in most of these dead animals the medium extended down the lumbar peripheral nerves for distances of 2 to 4 cm. after an interval of one or two hours.

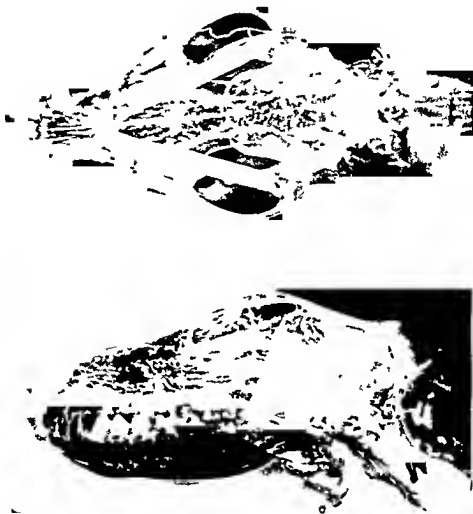


Fig. 8.—Radiographs of the head of a dog taken five hours after intracranial injection by cisternal puncture of ethyl iodophenylvalerate, a substance similar physically to iodobenzene. The medium has extended through the cribriform plate into the nasal and cervical lymphatics. In the dorsoventral view the valve structures of the lymphatics are visualized.

In another series of experiments media were instilled into the intracranial subarachnoid space under physiologic pressures. Rapid extension along the optic nerve and through the cribriform plate was observed. In the latter case the media flowed into the nasopharyngeal lymphatics, cervical lymph nodes

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raphy it is conceivable that unusual prolongations may account occasionally for short extensions of injected media but never for actual communication with the perineural spaces.

In Case 2 there was a complete subarachnoid block only a little above the point of injection and the termination of the lumbar cistern. Abnormal factors to account for the uniform extension of the medium into the nerve roots include (1) anatomic changes which may have developed as a result of a chronically obstructed subarachnoid space (2) pressure alterations produced by the injection of additional fluid into a small closed space and (3) injection directly into a nerve root rather than into the subarachnoid space. The first and second of these possibilities seem to offer the most plausible explanations.

In Case 3 there was no unequivocal evidence that most of the pantopaque was ever in the subarachnoid space. The original myelogram showed the opaque oil in essentially the same areas as the final one taken five months later. The most probable explanation in this case is therefore that the medium was injected to a large extent outside the subarachnoid space possibly subdurally.

The radiographic evidence in Case 4 indicated that the injection was made well outside the main body of the subarachnoid space presumably into the perineural spaces of a nerve root. As a result the pantopaque extended into the subarachnoid and subdural spaces and peripherally to the lumbosacral plexus. From the latter area it extravasated into other perineural spaces to fill portions of all the nerve trunks uniting at the plexus. Support for this concept can be derived from the fact that the nerves filled only on the side of the injection. This behavior is analogous to the results obtained experimentally in numerous injections of peripheral nerves which is well illustrated by Fig. 5.

These clinical experiences are similar to other published cases^{1,2} about which there has been speculation concerning the mode of absorption or escape of media from the lumbar cistern. It has been suggested by Maltby and Pendergrass¹ that rapid escape along the nerve roots seems to indicate passage through pre-existing channels. Others^{3,4} have considered from experimental and pathologic evidence that such mechanisms function prominently in the absorption of cerebrospinal fluid. The evidence collected from the clinical cases and laboratory experiments reported here does not support a free communication between the subarachnoid space and the perineural spaces of peripheral nerves under normal conditions. The results indicate rather that injected radiopaque oils escape from the lumbar subarachnoid space only under distinctly abnormal circumstances such as local anatomic abnormality or injection irregularity.

SUMMARY

In a series of 200 consecutive myelograms four cases were encountered in which the injected pantopaque extended outside the normal confines of the subarachnoid space apparently along the nerve roots. These phenomena have been correlated with results obtained experimentally in the study of the ex-

and periesophageal lymphatics and were recovered from the nasal secretions. The final stage of one such experiment in which ethyl iodophenylvalerate was used is shown in Fig 7. Most of the media used for this purpose were too irritating for chronic studies but pantopaque did not appear to have deleterious effects.

Experiments were devised also to illustrate the behavior of media under increased pressure in the lumbar subarachnoid space. The lumbar cisterns of dogs were cannulated and media run in under increasing pressures. No extension was observed until the lumbar cistern was ligated 5 cm proximal to the cannula and the pressure elevated to over 200 mm of Hg. Extravasation of media took place long before this pressure was reached and in only one instance was extension beyond the dorsal root ganglion observed in a living dog (Fig 8).

DISCUSSION

The experimental observations reported here shed some light on the behavior of radiopaque oils in the subarachnoid space. Under normal pressures a distinct difference was apparent between the behavior of media in the intracranial and in the intraspinal spaces. From the intracranial space the materials exited readily and under physiologic pressure through the cribriform plate into the nasal secretions and cervical lymphatic system. From the lumbar cistern extension of the radiopaque materials was never observed under physiologic conditions but did occur into the perineural spaces when excessive pressures were applied or the animal was killed.

The peripheral injection experiments serve to clarify somewhat the structure and communications of the perineural spaces. They appear to be connective tissue planes organized from the dural perineural sheath. These form discrete channels in such a fashion as to subdivide the progressively branching nerve into longitudinal compartments supporting axis cylinder extensions. Evidence favoring a physiologic current of fluid in these spaces was not obtained as media extended only under direct injection pressure or very slowly in an active animal. In the latter case flow occurred centripetally or in the opposite direction to that which would be expected if cerebrospinal fluid normally entered perineural channels from the subarachnoid system. Further such anatomic communication was not observed in serial sections of the dural penetrations of many roots. Finally media injected peripherally always entered the subarachnoid space from dural perineural clefts apparently by break through across the arachnoid.

Clinically evidence is lacking for physical communication normally between the spinal subarachnoid space and peripheral nerves. The four abnormal myelograms show that extension of media can occur and this suggests that communication does develop under unusual circumstances.

Case 1 presented a definite anatomic abnormality. It was notable here that although the medium extended well beyond the normal confines of the subarachnoid space it did not continue out the nerve in the perineural spaces. Since some variation in size of axillary pouches is normally seen in myelogram

raphy it is conceivable that unusual prolongations may account occasionally for short extensions of injected media but never for actual communication with the perineural spaces.

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THE EFFECT OF DIBENAMINE ON AUTONOMIC STIMULATION

F A SIMFONE, M D, AND S J SARNOFF, M D, BOSTON, MASS

(From The Surgical Research Laboratories of Harvard University at the Massachusetts General Hospital)

SIR HENRY DALE,¹ in 1905, reported that ergot extracts possessed the property of reversing the positive action of adrenalin. That same year Sollman and Brown² made a similar observation independently, and, in 1906, Dale³ published his classical paper "On Some Physiological Actions of Ergot." In it, he demonstrated the reversal of the pressor action of adrenalin on the blood pressure after the injection of active extracts of ergot. Since those early investigations, physiologists have used ergot extracts (ergotoxine) and similar compounds as tools for the study of autonomic neuroeffector systems and clinicians have tried to use the drugs therapeutically in hypertension and vaso-spastic conditions.

A number of drugs have been developed which have properties similar to those of ergotoxine. The best known are yohimbine, ethyl yohimbine, and the dioxane group synthesized by Fontneau, the most extensively studied of which is piperidinomethylbenzodioxane (933F). Like ergotoxine, they do inhibit or depress the positive action of adrenalin but the dosages required are such that the side effects caused by them preclude their use in the clinic.

Most recently Nickerson and Goodman⁴ reported a "new drug," dibenamine (Fig 1) which has properties similar to those of the drugs just mentioned and which was thought to have possible clinical applications. It is well recognized that yohimbine and

of adrenalin than they a

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know whether or not the drug blocks the effects of sympathetic nerve excitation as well as the effects of adrenalin, studies were undertaken to learn more about the physiologic properties of dibenamine.

METHOD

Experiments were performed upon sixteen cats of both sexes. Dialurethane* was used for anesthesia (0.75 to 0.80 c.c. per kilogram intraperitoneally). Records of the contraction of the smooth muscle of the nictitating membrane were made by attaching the right nictitating membrane to a recording lever writing with tenfold magnification on a slowly moving smoked drum. Blood pressures were recorded from the left carotid artery. The nictitating membranes were disconnected from the central nervous system by severing the cervical sympathetic trunk. Both vagi were divided in the neck. In experi

¹⁹⁴⁷ Presented at the meeting of the Society of University Surgeons, Boston, Mass., Feb. 13-15

*Manufactured by Ciba Pharmaceutical Products Inc., Summit, N. J.

ments concerning the effects of sympathin liberated from the heart this organ was denervated by dividing both vagi in the neck and by severing the communicating rami between the stellate ganglion and the first four thoracic nerves bilaterally. The adrenal glands were excluded from the circulation. Shielded silver electrodes were used to stimulate the cervical sympathetic trunk in the neck and the cardiac nerve in the thorax. When the thorax was opened properly adjusted artificial respiration was used through a tracheal cannula which was inserted routinely. The stimulator used was an electronic one which permitted varying the duration, intensity, and frequency of the shocks.

Intravenous injections were made into the long saphenous vein exposed in the right thigh or bilaterally when needed. The dibenamine was injected in volumes of 10 c.c. containing the dose to be used in physiologic saline solution. The stock solution contained 50 mg. per cubic centimeter in acidified 50 per cent ethyl alcohol. Adrenalin was prepared in dilutions of 1:20000 or 1:25000 in physiologic saline solution.

In the sympathin experiments for which the nictitating membrane was used as a test organ the membrane was previously sensitized by postganglionic denervation done twelve to seventeen days before the experiment.

(N,N-Dibenzyl- β -Chloroethyl amine)

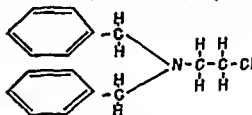


Fig. 1—Structural formula for Dibenamine

RESULTS

1 *The Direct Effect of Dibenamine Upon the Blood Pressure and Upon the Nictitating Membrane*—Fig. 2 represents the effect of dibenamine injected intravenously upon the blood pressure and upon the smooth muscle in the nictitating membrane of the cat. There was an initial rise of the blood pressure during the period of injection but after the injection within a period of five minutes the blood pressure had dropped to a level 20 mm. of mercury below the original pressure. In some instances the fall in blood pressure was 40 to 60 mm. of mercury.

Fig. 2 demonstrates also that the smooth muscle within the nictitating membrane is not affected directly by the drug. If anything there is a very slight relaxation of the muscle.

2 *The Effect of Dibenamine Upon the Sustained Contraction of the Nictitating Membrane and the Hypertension Induced by the Constant Intravenous Injection of Adrenalin*—Fig. 3 illustrates the effect of the injection of diben

amine upon the rise in blood pressure and the contraction of the nictitating membrane caused by the intravenous injection of 1 20000 adrenalin at a constant rate of 12 drops per minute. There is no immediate effect upon the contracted nictitating membrane, while the blood pressure drops quite promptly



Fig 2—Direct effect of dibenamine upon blood pressure (upper tracing) and nictitating membrane (lower tracing). Cervical sympathetics and vagi severed in the neck. Time signal 5 seconds. Double intervals are 60 seconds apart. Dibenamine (30 mg per kilogram injected during interval of approximately 80 seconds, lowermost record).

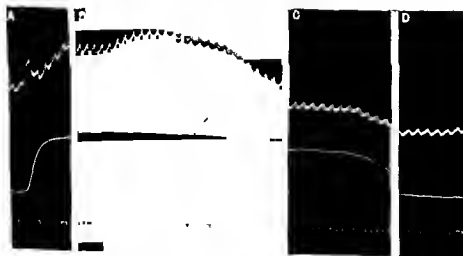


Fig 3—Effect of dibenamine upon the time.
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to its initial level and shortly afterward to a level well below the initial blood pressure. Meanwhile, there is a slight drop in the contraction of the nictitating membrane but it does not return to the resting level until five minutes after cessation of the injection. If the adrenalin infusion is continued long enough, the membrane does fall to its resting level but it may take ten to fifteen minutes to do so.

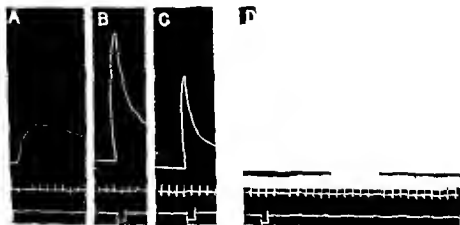
3 *The Effect of Dibenamine Upon the Sustained Contraction of the Nictitating Membrane Induced by Excitation of the Cervical Sympathetic Trunk*—Fig 4 illustrates the action of dibenamine upon the nictitating membrane contracted by stimulation of the cervical sympathetic trunk with maximal shocks at the rate of 20 per second. There is a slight but prompt fall in the degree of contraction during the injection but the fall does not continue at this rapid rate. Instead, the membrane relaxes very slowly—much more slowly than in the case of the contraction due to adrenalin.



Fig 4—Effect of dibenamine upon contraction of nictitating membrane induced by electric stimulation of cervical sympathetic by maximal shocks of one sigma duration and at frequency of 20 per second. Dibenamine (10 mg per kilogram) injected during an interval of 100 seconds as indicated by signal.

4 *Comparison of the Action of Dibenamine on the Effects of Stimulation of the Nictitating Membrane by Excitation of the Cervical Sympathetic and by the Injection of Standard Doses of Adrenalin*—Figs 5, 6, and 7 illustrate the blocking action of dibenamine on the effect of sympathetic nerve stimulation and on the effect of adrenalin. The nearly complete blocking of the action of adrenalin is seen by comparing sections A and D of Fig 5. The contraction in response to nerve stimulation is affected much less by dibenamine than is the contraction caused by adrenalin (see sections B and C of Fig 5). Fig 6 shows an absolute block of the action of adrenalin (see sections B and D, Fig 6) while the contraction due to stimulation of the cervical sympathetic is affected very much less (sections A, C, and E, Fig 6). This relationship holds even though the adrenalin response before dibenamine is administered is greater than the response to nerve stimulation. Fig 7 shows the action of dibenamine

in blocking the responses of the nictitating membrane and of the blood pressure to adrenalin and in blocking the response of the nictitating membrane to stimulation of the cervical sympathetic. The drop in the blood pressure after the administration of dibenamine is noteworthy. The figure illustrates again that the responses to adrenalin are blocked more quickly and more effectively than the responses to nerve stimulation. It may be noted further, that the effect of adrenalin upon the blood pressure is blocked sooner than the effect upon the membrane.



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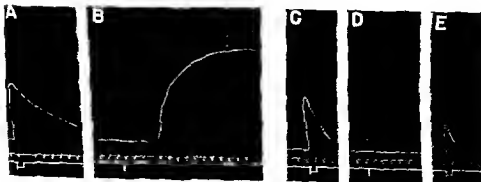


FIG. 6.—Effect of dibenamine upon contractions of nictitating membrane in response to adrenalin and to electric stimulation of cervical sympathetic. A Response of unsensitized nictitating membrane to electric stimulation (five maximal shocks per second for 5 seconds). E

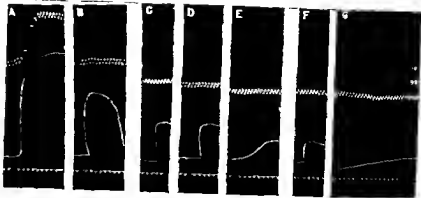


Fig 7—Responses of blood pressure (top record) and of nictitating membrane (next to top record) to adrenalin and sympathetic nerve stimulation.

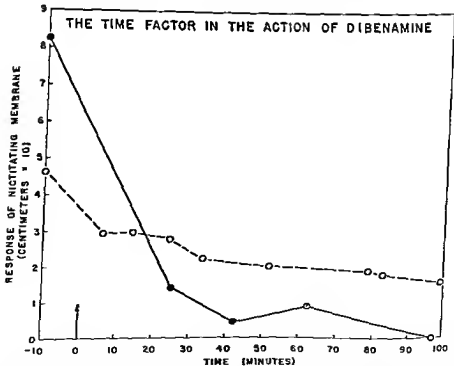


Fig 8—Time factor in action of dibenamine in a typical experiment. Broken line represents responses of nictitating membrane to electric stimulation (twenty maximal shocks per second for 5 seconds). Solid line represents responses of nictitating membrane to adrenalin injected intravenously. For dosages of adrenalin see text.

Fig 8 demonstrates graphically the differences indicated in the records. The effect of adrenalin is promptly and completely blocked. The contractions prior to sixty minutes were obtained with injections of 1 c.c. of 1:25000 adren

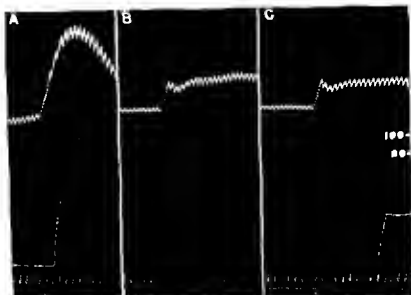


Fig 9—Responses of blood pressure (top record) and of nictitating membrane (next to top record) sensitized by intravenously for one minute. Resulting card

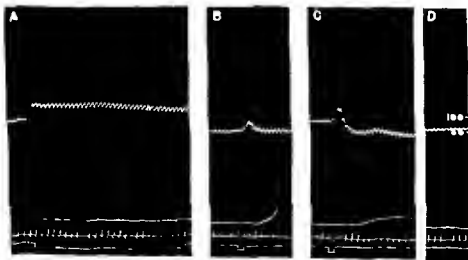


Fig 10—Same experiment as Fig. 9 after injection of dibenamine (20 mg. per kilogram). A Responses to same stimulus as in Fig. 9 B ten minutes after injection of dibenamine. B Responses to same dose of adrenalin as in 9A 15 minutes after injection of dibenamine. C and D Responses to same stimulus as in B 5 minutes later (an interval of 4 minutes cut out between C and D)

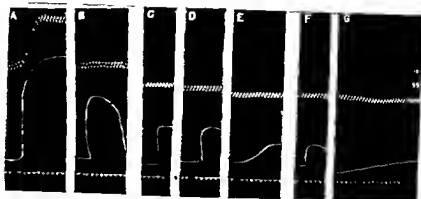


Fig 7.—Responses of blood pressure (see text).

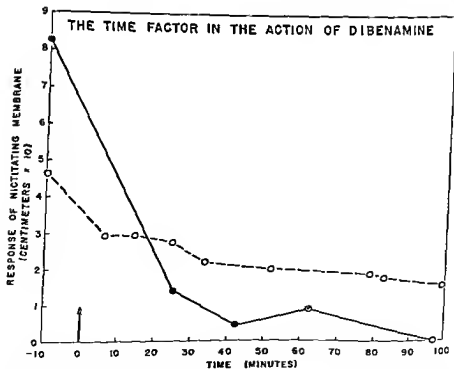


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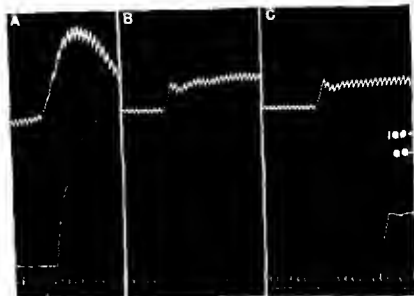


Fig 9—Responses of blood pressure (top record) and of nictitating membrane (next to top record) to same stimulus as in Fig 8. Nictitating membrane was days previously. A Responses to injection of adrenalin. B Responses to stimulation of right cardiac nerve. C Responses to same stimulus as in B (see text).

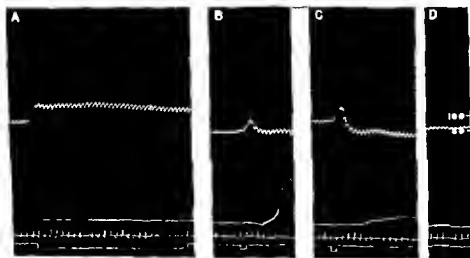


Fig 10—Same experiment as Fig 9 after injection of dibenamine (20 mg per kilogram). A Responses to same stimulus as in Fig 9. B ten minutes after injection of dibenamine. C Responses to same dose of adrenalin as in 9A 15 minutes after injection of dibenamine. D Responses to same stimulus as in B 5 minutes later (an interval of 4 minutes cut out between C and D).

also, the two points beyond the sixty minute mark were obtained with 1 cc volumes of 1:1000 adrenalin. The blocking action of the drug upon the responses to sympathetic nerve stimulation develops slowly and is incomplete.

5 *The Effect of Dibenzamine on the Response of the Nictitating Membrane to Circulating Sympathin*—Fig. 9 illustrates the responses of the sensitized nictitating membrane and of the blood pressure to the injection of 0.5 cc of 1:25000 adrenalin in *A* and to stimulation of the cardiac nerve for one minute periods in *B* and *C*. During the stimulation the heart rate increased from a basal of 142 beats per minute to 204 beats per minute. The degree of tachycardia resulting from the stimulation was the same in *B* and *C*. Fig. 10 shows the responses to the same stimuli after the injection of 20 mg of dibenzamine per kilogram intravenously. At *A*, the cardiac nerve was stimulated for two minutes, instead of one. The same tachycardia was obtained as in Fig. 9 *B* and *C*, but there was no contraction of the nictitating membrane. In *B* Fig. 10, there is still some response to adrenalin. Section *C* Fig. 10 illustrates that the response of the nictitating membrane to adrenalin is nearly abolished and that the response of the blood pressure is biphasic. Circulating sympathin then, appears to be blocked as effectively as adrenalin if not more so.

DISCUSSION

The data presented here demonstrate that dibenzamine blocks the positive action of adrenalin and thereby unmasks its negative effects. The action of circulating sympathin is likewise blocked by the drug. This effect is probably not the result of failure of sympathin to enter the circulation for Nickerson and Goodman² have reported acceleration of the denervated heart when the splanchnic nerves are stimulated under the influence of dibenzamine and in the absence of the adrenal glands.

The blocking action is not as great upon the effects of nerve stimulation as it is upon the effects of circulating adrenalin and sympathin. Cardio acceleration from excitation of the cardiac nerve is not affected at all and while diminished the contraction of the nictitating membrane in response to stimulation of the cervical sympathetic is not abolished. These findings are comparable with the effects of 933F (Cannon and Rosenbluth⁴) and ethyl yohimbine (Yonkman, Stillwell and Jeremiah⁵).

The effect of dibenzamine is not immediate. Although some modification of the action of adrenalin is demonstrable within five minutes from the time dibenzamine is injected, often the maximum effect is not obtained until thirty minutes or more have elapsed. This suggests that the effect of the drug is not directly upon adrenalin or sympathin but rather on some substance intervening between the mediator and the contractile mechanism or possibly on the contractile mechanism itself. In support of this opinion may be mentioned the evidence presented by Nickerson and Goodman² that dibenzamine has no deleterious effect upon adrenalin *in vitro*. This finding differs from the observation of Morrison and Lissak⁶ that 933F does have a destructive action upon adrenalin in the test tube.

If dibenamine does not act directly upon adrenalin or sympathin what is the mechanism of its action? Cannon and Rosenblueth⁶ postulated that 933F and similar substances may act by decreasing the permeability of the effector cell membranes. Such a theory would readily explain the blocking effect upon circulating adrenalin, adrenine or sympathin, all of which must pass through cell boundaries in order to reach the effector cells. Considered in the light of the premise that smooth muscle is not a syncytium and that only some smooth muscle cells are directly innervated by nerve fibers (Cannon and Rosenblueth⁶) the theory would explain the fact that the effects of sympathetic nerve stimulation are diminished but not abolished by the drug for the innervated cells would contract in response to sympathin produced within their cell boundaries but the uninnervated smooth muscle cells which depend for stimulation upon the diffusion into them of sympathin from the innervated cells would not contract.

A strong argument against the theory that dibenamine acts by decreasing permeability of effector cells however is the fact that when dosage response curves are plotted instead of a shift of the curve to the right which would obtain if the permeability of cells had decreased and larger doses are therefore needed to produce the same response there is a lowering of the asymptote of the curve (Acheson and Farah⁹). In other words it is impossible to produce as great a response in the smooth muscle after as before dibenamine regardless of how much the chemical or electrical stimulus is increased.

Dibenamine might act by modifying an intermediate substance with which the chemical mediator must combine in order to exert its effects. It is noteworthy in this regard that the drug does abolish the action upon the nictitating membrane of circulating sympathin E which presumably has already combined with an intermediate substance (Rosenblueth¹⁰). It is difficult further more to explain on such a theory the difference between the blocking effect against adrenalin and that against locally produced sympathin. One would need to assume that locally produced sympathin is produced in extraordinary concentrations locally and is therefore more effective purely by the mass action effect or that it has a greater affinity than adrenalin for the receptors in the contractile mechanism.

Finally the data presented might be used to support a theory that dibenamine acts directly upon the contractile mechanism itself. In its favor are the facts that (1) dibenamine is fundamentally a tissue poison (Nickerson and Goodman) (2) its action in blocking adrenergic effects is not immediate and (3) it is impossible to obtain as great a response after dibenamine as before regardless of the dosage of adrenalin or the frequency of stimulation employed. Again however there is difficulty in explaining the difference between the effect upon the action of adrenalin and that upon the action of locally produced sympathin.

It is impossible with what data are available to distinguish between the theories cited with finality or to state that any is the correct one. It is reasonable however to discount theories depending upon changes in permeability of the effectors or upon destruction of the mediator since dibenamine does not

destroy adrenalin in the test tube (Nickerson and Goodman⁵), and does not block the action of adrenalin on the heart (Acheson and Farah⁶). The theory that the drug acts directly upon the contractile mechanism itself fits the facts best.

One would expect that since dibenamine does have a prolonged blocking action against the positive effects of adrenalin and, at least partly, against the positive effects of sympathetic nerve stimulation, it would find wide clinical application. It could be useful in the treatment of hypertension and vasospastic conditions and indeed has been used in such conditions (Goodman¹¹). Substances with similar properties (piperidinomethylbenzodioxane, yohimbine, ergotoxine) have not been useful therapeutically because of the undesirable side effects produced by the dosages needed.

In this clinic dibenamine was used twenty three times and the following side effects were observed: (1) local venous thrombosis at the site of injection; (2) nausea and vomiting in six patients of slight to moderate degree lasting six to twenty four hours; (3) two transient toxic psychoses; and (4) coma and loss of sphincteric control lasting for one hour in a man in whom epilepsy could not be ruled out. The data that we obtained indicate that dibenamine reverses the pressor effect of adrenalin in the normal human being as it does in the cat.

While this clinical experience has not been extensive the severity and frequency of the reactions have made it unwise to use the drug therapeutically until more is learned about the mechanism and methods for controlling the undesirable effects.

As a diagnostic agent, the drug might find application in the diagnosis of pheochromocytoma in hypertension. One would expect the drug to have a greater blood pressure lowering effect in such hormonal hypertension than in other types of hypertension. Blockage by dibenamine of the blood pressure rise induced by histamine in patients with hypertension would be especially suggestive of pheochromocytoma (Both and Kvale¹²).

Nickerson and Goodman⁵ reported that dibenamine can prevent the ventricular fibrillation which occurs under cyclopropane anesthesia when adrenalin is administered. This fact might find application clinically. Since dibenamine does not abolish the chronotropic effect of adrenalin upon the heart this observation suggests that adrenalin produces ventricular fibrillation by some mechanism which is blocked by dibenamine but is different from its chronotropic effect.

SUMMARY

1 The blocking action of dibenamine upon the effects of adrenalin and locally produced sympathin develops slowly. This action of dibenamine upon the responses to adrenalin begins to appear soon after injection of the drug but often does not reach a maximum until thirty or more minutes after the injection (Fig 8).

2 The blocking action of dibenamine upon the responses to sympathetic nerve stimulation develops more slowly and less completely than its blocking action upon the responses to adrenalin (Figs 5 6 7, and 8)

3 Circulating sympathin is blocked as effectively as adrenalin by dibenamine if not more so (Figs 10 and 11)

4 Because the drug has a prolonged blocking effect upon the positive responses to adrenalin and to sympathetic nerve stimulation it could find extensive clinical application (hypertension vasospastic diseases of the extremities cardiac arrhythmias) if its untoward side effects can be eliminated

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FACTORS IN THE REDUCTION OF MORTALITY IN ACUTE APPENDICITIS

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MANY clinics are reporting a marked lowering in the mortality rate from acute appendicitis in the last few years^{1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12}. It is generally accepted that chemotherapy is responsible for the improvement but specific proof for this belief is singularly lacking due to the multiplicity of factors affecting mortality and the simultaneous improvement in other aspects of treatment. The experience at the Peter Bent Brigham Hospital is in accord with that of the country at large in showing a striking decrease in the mortality rate from 1941 through 1945 (Table I). During this time there was only one death in 382 consecutive cases of acute appendicitis although on the basis of previous experience from twelve to fifteen deaths were to be expected. Studies from this hospital covering the years up to 1941^{1, 2, 3} showed no appreciable change in mortality for twenty years but form a particularly useful background for determining which specific changes have effected the improvement.

In order to determine the responsible factors a detailed comparison has been instituted between the 517 patients operated upon from 1936 through 1940 and the 382 patients operated upon from 1941 through 1945. Both series of patients have been selected and analyzed by identical methods. Each represents a consecutive series of operative cases*. In each series patients below the age of 12 years are rare (the usual lower age limit for the hospital). In each series patients with tuberculosis, actinomycosis, carcinoma or carcinosarcoma of appendix or cecum have been excluded. In each individual case there has been an histologic diagnosis of acute appendicitis when the appendix was removed or obvious gross pus at operation in instances in which a large abscess made immediate removal of the appendix impossible.

The cases have been divided into three groups as follows:

(1) *Acute perforated appendicitis* if a gross perforation was described by surgeon or pathologist. No attempt has been made to define the precise extent of the peritonitis desirable though this would be a careful study of operative notes by many different surgeons of varying experience and powers of observation showed that such a differentiation would not be reliable.

(2) *Appendical abscess* if there was localized pus at operation with or without gross perforation of the appendix.

(3) *Acute unruptured appendicitis* in the absence of gross perforation or localized pus. This group includes many patients with peritonitis and positive peritoneal culture without perforation. Again no reliable method of including patients with such peritonitis with the perforated group appeared to be avail-

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*There were no deaths from 1941 through 1945 in patients not operated upon.

TABLE I ACUTE APPENDICITIS—MORTALITY RATE BY FIVE YEAR PERIODS, 1913-1945

YEARS	TOTAL CASES	DEATHS	MORTALITY (%)
1913-1920	475	26	5.5
1921-1925	427	17	4.0
1926-1930	402	15	3.7
1931-1935	375	17	4.5
1936-1940	517	25	4.8
1941-1945	392	1	0.3

able and it seemed best to classify these with the ruptured group. Also included in this group are those cases in which the appendix was broken in removal.

Although this grouping of acute appendicitis is not ideal, it has the virtue of easy application, and minimal dependence upon the personal observations of many different surgeons concerning the extent or type of peritonitis present which in a properly executed operation is often not determined.

TABLE II ACUTE APPENDICITIS—CLASSIFICATION OF CASES, 1913-1945

YEARS	ACUTE UNRUPTURED APPENDICITIS		ACUTE PERFORATED APPENDICITIS		APPENDICULAR ABSCESS	
	CASES	% OF TOTAL	CASES	% OF TOTAL	CASES	% OF TOTAL
1936-1940	400	78.3	82	15.9	30	5.8
1941-1945	303	79.3	55	14.4	24	6.3
1913-1945	1908	74.5	395	15.3	271	10.6

It is beyond argument that the vast majority of deaths occur after perforation or abscess formation has taken place in the course of acute appendicitis. The first point of interest, therefore, is the relative frequency of "complicated" appendicitis in the two five year periods. Table II presents the percentage of cases of each type of appendicitis for the entire period 1913-1945, as well as for the five year periods under consideration. Although there has been some decrease in the number of patients with abscess or perforation in the past five years, the proportion is not significantly lower than it was in 1936 through 1940. Table III carries this finding one step further and demonstrates a decrease in the mortality in 1941 through 1945 for each type of appendicitis, most marked in the group with perforation.

Since in the past the combined groups of perforated appendicitis or appendicular abscess have had a mortality rate ten to fifteen times greater than un-

TABLE III ACUTE APPENDICITIS—GROUP MORTALITY RATE BY FIVE YEAR PERIODS, 1913-1945*

YEARS	ACUTE UNRUPTURED APPENDICITIS		ACUTE PERFORATED APPENDICITIS		APPENDICULAR ABSCESS	
	CASES	MORTALITY (%)	CASES	MORTALITY (%)	CASES	MORTALITY (%)
1913-1920	294	1.4	97	17.5	84	6.0
1921-1925	315	0.6	57	21.9	52	7.7
1926-1930	301	1.3	56	12.5	41	2.4
1931-1935	275	2.1	50	14.0	40	10.0
1936-1940	405	1.0	81	18.5	30	13.3
1941-1945	303	0.0	55	0.0	24	4.2
1913-1945	1907	1.0	394	14.7	271	7.0

*Two anesthesia deaths omitted (none 1941-1945)

TABLE IV ACUTE APPENDICITIS—FACTORS ACTING PRIOR TO OPERATION
APPENDICITIS WITH GROSS PERFORATION OR ABSCESS

	110 CASES (%) (1936-1940)	79 CASES (%) (1941-1945)
Age of patient 50 years or more	35	9
Symptoms for 48 hours or more before hospitalization	53	71
Definitely received a cathartic	47	3*
Delay in hospital more than 6 hours for diagnosis	12	14
Admission pulse 100 or more	57	36
Admission temperature 102° F (R) or more	36	30
Pulse 100 or more and temperature 102° F (R) or more	30	25

*Significant difference

ruptured appendicitis it is appropriate to focus our attention on these two groups and to scrutinize with care the various factors which may have bearing on their far greater threat to life. To accomplish this the patients with perforation or abscess have been grouped together for 1936 through 1940 and 1941 through 1945 and then cross analyzed with respect to three sets of factors: those acting prior to operation, those acting at the time of operation, and those acting after operation. The results appear in Tables IV, V, and VIII.

In Table IV it is seen that there is close agreement in the frequency of those factors which may be regarded as representing the preoperative risk or measuring the constitutional response of the patient to his illness. The only significant* decrease occurred in those patients known to have received a cathartic; not too much emphasis may be placed upon this since during the war years the recorded history was frequently rather sketchy. Furthermore the chief damage caused by cathartics is in the production of the complications which all of these cases had.

In Table V it may be seen that there are several significant differences between the groups when factors acting at the time of operation are analyzed. The increased use of ether anesthesia in these complicated cases is probably

TABLE V ACUTE APPENDICITIS—FACTORS ACTING AT TIME OF OPERATION
APPENDICITIS WITH GROSS PERFORATION OR ABSCESS

	110 CASES (%) (1936-1940)	79 CASES (%) (1941-1945)
Ether anesthesia	64	81*
Operation by resident staff	80	71
McBurney incision	66	72
Duration of operation 1 hour or more	9	63*
Positive peritoneal culture (when taken)	40	80
Local sulfanilamide wound or peritoneum	7	47*
Drainage of peritoneal cavity	61	35*

*Significant difference

*The following formula has been used for determining a significant difference between frequency rates in two series:

$$\sqrt{\frac{A \times (100-A)}{X} \text{ plus } \frac{B \times (100-B)}{Y}}$$
 is greater than 2

No. of Cases $\frac{A}{X}$ Series 1 Frequency $A\%$ No. of Cases $\frac{B}{Y}$ Series 2 Frequency $B\%$

Suppose A greater than B the difference is then A-B. This difference is significant if

TABLE VI ACUTE APPENDICITIS—DECREASING INCIDENCE OF DRAINAGE IN ACUTE UNRUPTURED APPENDICITIS

YEARS	DRAINED (%)	MORTALITY % (ALL CASES)
1913 1920	4.5	14
1921 1925	36.5	0.3
1926 1930	15.7	1.3
1931 1935	17.2	2.1
1936 1940	4.9	1.0
1941 1945	1.0	0.0

related to the increased duration of operation. During the war years the house staff was less thoroughly trained than formerly, and the longer operations are evidence of inexperience coupled with the proper exercise of care and gentleness rather than speed. A short acting spinal anesthesia such as procaine was likely to prove insufficient and there was evidently reluctance toward using the longer acting ones. Neither of these factors can be supposed to have reduced the mortality rate; most surgeons agree that spinal anesthesia is preferable to ether for these patients and all agree that reasonably rapid surgery is desirable. There is a sharp increase in the use of sulfanilamide locally in the peritoneum or wound, but it is felt that this is not a responsible factor, or even of much importance, in only two instances was it used without accompanying systemic chemotherapy and in only one case since 1943 was it used at all. It has now been completely abandoned in this hospital. (It is realized that some surgeons still lay great store by the local use of sulfonamides.)

There is also a sharp drop in the incidence of peritoneal drainage. Table VI shows the consistent trend toward less drainage of acute unruptured appendicitis through the years and Table VII shows the expansion of this policy to include all types of appendicitis. Although it cannot be proved that non-drainage prevents deaths at least the decrease in its use is indicated. Our experience demonstrates that it is unnecessary to use drains in the majority of complicated cases. Even abscesses may be closed without drainage, if the appendix is removed and the abscess either is very minute or its walls can be seen to collapse after the pus has been evacuated. On the other hand it is my belief that properly employed drains per se are rarely an actual cause of death or even contribute to fatalities to any marked degree, although it is recognized that some able surgeons hold a contrary view. The high mortality reported everywhere in cases in which drainage was used is far more likely to be related to the fact that it is used in the worst cases rather than to the injury of the drains themselves.

Our clinic has stressed for many years the importance of the McBurney incision as the one of choice for acute appendicitis; exceptions to this rule are

TABLE VII ACUTE APPENDICITIS—INCIDENCE OF PERITONEAL DRAINAGE

	DRAINED (%) (1936 1940)	DRAINED (%) (1941 1945)
Acute unruptured appendicitis	5	1
Acute perforated appendicitis	53	25
Appendiceal abscess	81	58
All cases	14	8

pelvic appendicitis and acute appendicitis in females if the diagnosis is doubtful. There has been a slight but not significant increase in the frequency with which this incision has been used in the last five year period under consideration.

Table VIII, which analyzes factors acting after operation, holds the chief clue, in my opinion, to the lessening of fatalities. The greatest difference in any of the factors considered is the tremendous increase in the systemic use of the sulfonamides, rising from 14 to 85 per cent. Sulfathiazole was the drug first used in the 1941 through 1945 group, but since about 1942 sulfadiazine was used almost exclusively. The drugs were often given preoperatively with the fluids administered in the preparation of the sickest patients. Penicillin was not available for general use in our hospital until the latter part of 1945 and so was given in only four patients. It is now used regularly in patients with peritonitis, and its proper place in treatment is being evaluated. At any rate it played an insignificant role in the years under consideration.

TABLE VIII ACUTE APPENDICITIS—FACTORS ACTING AFTER OPERATION
APPENDICITIS WITH GROSS PERFORATION OR ABSCESS

	110 CASES (%) (1936-1940)	8 CASES (%) (1941-1945)
Received systemic sulfonamides	14	85*
Received systemic penicillin	—	5
Plasma or blood transfusion	25	37
Gastrointestinal siphonage	47	77*

*Significant difference

There is an increase in the use of blood and plasma not significant for the size of the series. There is a significant increase in the use of gastrointestinal siphonage. Undoubtedly this has helped save some lives. However a study of all our fatalities from acute appendicitis² showed that only 10 per cent died as a direct result of mechanical intestinal obstruction or paralytic ileus, whereas nearly 70 per cent died as a result of intra abdominal sepsis. (Some 20 per cent died of other causes such as pulmonary embolism pneumonia etc.) While the proper use of siphonage is unquestionably an important feature of the treatment of peritonitis its point of action is not at the infection itself. Further more many patients have died in the past despite its use. For these reasons it is felt that gastrointestinal siphonage must be relegated to a role secondary to that of chemotherapy in reducing the fatalities.

REPORT OF FATAL CASE

1 S (Surgical No. 5510) a 70 year old white man was admitted to the hospital for the second time Sept. 28, 1945 complaining of right upper quadrant abdominal pain of with the same complaint. Recurrence of pain with anorexia and constipation brought the patient to the hospital again. Examination showed tenderness and resistance in the right upper quadrant extending to the right flank and percussion tenderness over the right lower ribs anteriorly. The diagnosis again was acute cholecystitis and after six days of expectant treatment the abdomen was opened through a right upper rectus muscle-splitting incision. The gall bladder was normal but there was an infrahepatic abscess of appendiceal origin. The cecum was malrotated and the appendix

ly behind it. Appendectomy with drainage was carried out. Postoperatively the patient did poorly. He was given sulfadiazine which was changed to penicillin in large dosage on the sixth postoperative day (40,000 units every two hours). He developed an intractable hypoproteinemia despite repeated blood and plasma transfusions, a wound infection with dehiscence, pulmonary edema and bronchopneumonia. He died on the thirteenth postoperative day.

Autopsy—There was a residual abscess retrocecaly, (despite drainage), acute bronchitis and bronchopneumonia and cellulitis of the abdominal wound. There was no generalized peritonitis.

Comment—Death must be regarded as primarily due to acute appendicitis with abscess formation although the hypoproteinemia and pulmonary complications finally tipped the balance.

SUMMARY

In the 382 patients operated upon for acute appendicitis in the years 1941 to 1945 at the Peter Bent Brigham Hospital there was only one death. This represents an unprecedented drop in mortality for this disease. An analysis shows that there was approximately the same proportion of complicated cases with perforation and abscess as there was in the preceding five years. From a detailed comparison of patients with perforation or abscess operated upon in 1936 through 1940 and in 1941 through 1945 it appears that the chief factor responsible for the great improvement in the latter group was the systemic use of sulfonamides; the more frequent use of gastrointestinal siphonage probably played a subsidiary role. There has been a slight increase in the frequency of the McBurney incision and a further reduction in the use of peritoneal drainage even in the complicated cases.

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Editorial

The Definition of a Surgical Resident

THE high priority given the certificate of the American Board of Surgery by the armed services; courts of workmen's compensation, and medical indemnity insurance has made recent graduates conscious of its desirability. When such certification is made a requisite for an appointment to a hospital staff, it becomes mandatory. For those who seek its certificate, the American Board of Surgery has expressed a preference for residency training to fulfill the requirements leading to examination. Consequently, a surgical residency has become the goal of most men who wish training in this field. The well established residencies in university clinics are few in number so cannot possibly fulfill the need. On the other hand, the graduate student is reluctant to spend time in a hospital and not receive "credit" for his work so "unapproved" hospitals have had difficulty in filling their resident staff in spite of the large number of those desiring such training. This has led to a rush for "approval" and to the creation of residencies that do not remotely resemble those that originated this system of training in the university clinics. Approval for internship is separated from that for residencies so that one finds smaller hospitals approved for resident training which do not have internships, nor do they have adequate libraries, research laboratories or ward services. The meaning of the term "resident surgeon" now has such widely different connotations that it is useless as a yardstick to evaluate proficiency.

The resident system of training in surgery was established in this country by Halsted. Originally his "first assistant" was resident for many years but later one or two years was the rule both at Johns Hopkins and in the other clinics that adopted this method. There was enough uniformity to say that a residency training consisted of a period of five to seven years divided as follows: After internship from three to five years were spent as an assistant resident. One year of this was often in an experimental laboratory or in surgical pathology. The remainder was spent in rotating through the various branches of surgery and often the assistant resident acted as resident in the surgical specialties. Occasionally, the assistant resident would spend a year in some other clinic or he might study abroad. By the time the residency was reached full responsibility could be given for the care of patients in the clinic. This resulted in the resident surgeon having the responsibility for 300 to 500 major operations during his term of service. He ended it a finished surgeon. How different this is from the training we now see in many so called "approved residencies." This

difference creates an urgent need to define what we mean by resident training in surgery, for unless this is done, conditions will become chaotic

The Society of University Surgeons has as a condition of membership the stipulation that a candidate must have completed an acceptable residency in surgery. It becomes a challenge to them to define what is meant by this. Such a definition would not be quibbling over words but would clarify our thinking on what is needed to elevate graduate education in surgery. If the Society can do this it will have rendered a service

—*Herman E. Pearse, M.D.*
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Review of Recent Meetings

MEETING OF THE SOCIETY OF UNIVERSITY SURGEONS

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THE eighth annual meeting of the Society of University Surgeons was held in Boston, Mass., Feb. 13, 14, and 15, 1947. Hosts to the Society were the Massachusetts General Hospital and the Peter Bent Brigham Hospital.

On the first day of the meeting, following welcoming remarks by Edward D. Churchill, the following papers were presented by the staff of the Massachusetts General Hospital and their associates:

An Effective 90 Second Surgical Scrub—Carl W. Walter

The Treatment of Compression of the Esophagus and Trachea Resulting From Abnormalities of the Great Vessels—Robert E. Gross

Recognition and Treatment of Subdural Hematomas in Infants and Children—Francis D. Ingraham

Favorable Results of Surgery in Recurrent Cancer of the Colon and Rectum—J. E. Dunphy

An Unusual Type of Congenital Duodenal Obstruction—Thomas W. Botsford

A Study of the Effects of Early Rising in the Postoperative Period—James B. Blodgett

The Influence of Estrogen on Advanced Carcinoma of the Breast—Ira T. Nathanson

The Diagnosis of Cancer by Cytological Means—Howard Ulfelder

Cancer of the Stomach—Ten Year Study—Claude E. Welch

Portal Hypertension—Treatment by End to Side Splenoportal Anastomosis With Preservation of the Kidney—Robert B. Linton

Intracarotid Pressure in Intracranial Aneurysm—William H. Sweet

The Hyperfunctioning Adenoma of the Thyroid—Oliver Cope

Peritoneal Irrigation for the Treatment of Acute Renal Failure—Howard A. Frank

The extracellular Space in Relation to Burn Therapy—Francis D. Moore

Recent Studies in Irreversible Shock—Arnold M. Seligman

The second and third days of the meeting were devoted to papers by members of the Society. In addition to those which are published in this issue of the JOURNAL, the following papers were presented:

Arteriovenous Fistula of the Lung—Report of Case Treated Successfully by Lobectomy—Edwin A. Lawrence, University of Utah

Implantation of the Pancreatic Duct in Resection of the Duodenum and Head of the Pancreas for Carcinoma—John T. Reynolds, University of Illinois

Experimental Production of Adenocarcinoma of the Stomach and Its Relationship to Gastritis—Edward L. Howes, Columbia University

The Role of Infection in Experimental Closed Loop Small Bowel Obstruction—Earle B. Mahoney, John Schilling, Walter Gunkler, and Harry Kingsley, University of Rochester

At the annual dinner the presidential address by Cobb Fitcher embraced the problem of the private practice of surgery in university hospitals.

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Original Communications

BENIGN CENTRAL CARTILAGINOUS TUMORS OF BONE

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(From the Bone Tumor Department, Memorial Hospital)

THIS communication is concerned with a study of a group of benign central tumors of bone which are derived from cartilage. It includes also the central chondromas and benign chondroblastomas which have been referred to in recent medical literature as "Codman's epiphyseal chondromatous giant cell tumors." The two groups will be considered separately.

CENTRAL CHONDROMA

The central chondroma or enchondroma is a benign lesion occurring mainly within the bone as contrasted with the osteochondroma or enchondroma which is chiefly cortical and projects beyond the normal confines of the bone. A series of twenty-two cases of central chondroma observed in the bone tumor department of Memorial Hospital forms the basis of this study.

Age—Although central chondroma probably has a long latent period during which its presence is not suspected, it is usually noticed between the ages of 10 and 30 years (see Table I).

Sex—Sex is of no apparent importance in this condition, twelve of the cases occurred in females and ten in males.

Bone Involved—The long bones were affected in all cases and extremity bones accounted for all but one—a rib (see Table II).

More than one third of the cases presented lesions of the phalanges and this is the most frequent tumor found in that location.

Clinical Manifestations—Simple chondroma may be completely symptomless. When it has altered the contour of the bone the patient may notice swelling or deformity. Pain, when present, is generally inconstant and mild. Disability is infrequent. Pathologic fracture, especially in phalangeal chondromas, is often the incident which gives rise to the recognition of the condition. Trauma which results in the fracture is often trivial and nearly always less severe than that which is responsible for simple fractures through normal bone. There was a history of antecedent injury in eight cases which led to the discovery

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of the tumor. The usual history was that of an injury followed by pain, swelling, and ecchymosis. However, the triviality of the symptoms is indicated by the fact that the patients often delayed several years before seeking treatment.

Etiology—As yet no completely satisfactory theory of the origin of central chondroma has been advanced. Disturbances in cartilage of a developmental nature may be an important factor. The concept that following injury to bone cartilage is found in the reparative process is not convincing as applied to the derivation of central chondroma.

Gross Appearance—The surgeon seldom finds it difficult to identify this tumor at operation. It lacks the gross appearance of tissue seen in simple cyst, giant cell tumor, or fibrous dysplasia. It presents a solid, whitish firm tumor completely filling the cavity and has a slightly gritty feel when attempts are made to remove it with the curette. At times calcific particles are seen and felt but it lacks the purely fibrous quality of fibrous dysplasia, the vascular reddish nature of giant cell tumor, or the fluid filled spaces of simple cyst. Myxomatous changes are not uncommon and it is probable that the extremely rare cases of pure myxoma of bone which have been reported are examples of degeneration of a central chondroma. While not encapsulated the lesion is usually rather definitely circumscribed and for this reason it is possible to remove it completely by painstaking curettage.

Microscopic Findings—The histologic appearance of this tumor is so characteristic that it should offer little difficulty to the experienced pathologist. Hyaline cartilage predominates. The cells are usually rounded but may vary in size and may become fusiform or stellate. Calcification may be seen in scattered areas.

Since there is a distinct tendency toward secondary chondrosarcomatous change and because this may not be evident in all parts of the tumor, it is

TABLE I

AGE (YEARS)	NUMBER OF CASES
Under 11	1
11 to 20	6
21 to 30	9
31 to 40	
41 to 50	1
51 to 60	0
61 to 70	1
71 to 80	1
Total	20

TABLE II

BONE INVOLVED	NUMBER OF CASES
Phalanx	8
Femur	4
Tibia	4
Humerus	2
Fibula	1
Metacarpal	1
Rib	1
Multiple (phalanges metacarpal fibula)	1
Total	22

necessary to bear in mind that a report of "benign chondroma" based on an examination of only a portion of the entire tumor can be misleading. It is of course obvious that a microscopic study should invariably be made of all portions of the tissue removed from any central bone lesion (Fig. 1).

X-Ray Findings—While the roentgenologist can frequently make a strong presumptive diagnosis of a central chondroma on the basis of a circumscribed area of radiolucency in the end of a long bone it is often possible to confuse the picture with that presented by bone cyst, giant cell tumor, and nonosteogenic fibroma of bone. We have seen cases in which a roentgenographic diagnosis of giant cell tumor was made without a biopsy and prolonged roentgen



Fig. 1. Histologic appearance of benign chondroma. Cartilage cells are lying in a matrix of hyaline material. The cells are uniform in size, shape and nuclear staining.

therapy given without apparent improvement. By the time the diagnosis of chondroma was confirmed by late histologic examination the effect of the radiation was such as to render a surgical attack impractical or actually hazardous. We believe therefore that any accessible central bone lesion deserves an exploration and complete extirpation by surgical means. This method assures a microscopic diagnosis and most important gives satisfactory results regardless of whether the condition is one of cyst, chondroma or giant cell tumor. In certain instances a central chondroma may closely resemble a chondrosarcoma or an osteolytic osteogenic sarcoma and it is therefore imperative that this issue be clearly decided before radical surgery is instituted.

Treatment—The treatment of central chondroma is surgical. For lesions in the rib, fibula and scapula resection of the entire tumor-bearing area is indicated. In the majority of cases involving other bones this will not be

practical and it is not essential since a thorough curettage with adequate exposure obtained by unroofing the cavity will yield satisfactory results*. When the involved area constitutes a considerable proportion of the thickness of the shaft of an essential long bone (femur, humerus, tibia, etc.) it is important to utilize bone chips obtained from the ilium or pencil grafts from the tibial cortex to fill the defect and to assure more complete and more rapid bone regeneration.

In occasional cases where curettage has been followed by one or more recurrences a segmental resection is an alternative to an amputation.

Recurrences will take place if the removal is incomplete but in this series only two of the twenty-two patients had a recurrence and both have been successfully managed by reoperation.

Four patients received roentgen therapy. In three of these (two lower femur and one upper tibia) the response was so unsatisfactory that a mid thigh amputation had to be performed in two, while in the third an aspiration biopsy disclosed that the condition had become sarcomatous. The fourth patient received preoperative irradiation of a rib tumor which was then resected.

TABLE III TREATMENT OF CENTRAL CHONDROMA

METHOD EMPLOYED	NUMBER OF CASES
Roentgen rays only	4
Surgery only	18
Excision	2
Curettage only	6
Curettage plus chips or tray grafts	6
Resection	1
Amputation	2
Roentgen rays and surgery	4
Amputation	3
Resection	1
Operation (curettage) elsewhere	1
Total	

Complications.—The course of these cases was singularly devoid of complications. Primary wound healing occurred in every instance and no late imperfections were observed. Pathologic fracture occurred in one case (metacarpal) while the patient was catching a baseball.

The end result was classified on an anatomic functional and economic basis. With a few exceptions two cases too recent for evaluation, three patients who died, and one in which amputation was performed, the results were uniformly good. The follow-up extended from one to fourteen years; in eight cases follow-up was for five or more years and in five of the latter for more than ten years.

CASE REPORTS

CASE 1.—A C, a 2-year-old woman, was admitted to Memorial Hospital on Sept. 13, 1930, with a history of intermittent pain over a period of four years. The first roentgenographic examination made three months prior to admission revealed a cystic area in the middle third of the left humerus. There had been no previous surgical or radium therapy. Local examination revealed a smooth, tender, spindle-shaped swelling of bone.

Following a curettage on Sept. 23, 1930, a pathologic diagnosis of central chondroma was made. Ten months later a recurrence was noted and a second curettage was performed on July 23, 1931, following which the pathologist reported atypical mucinous granulations, chronic osteitis, callous.

The patient remained practically symptom free for eight years, at the end of which time the pain recurred. Roentgenograms revealed reactivity in the mid humerus. She was readmitted to the hospital on June 4, 1934, for a third operation which consisted of an extensive exposure of the tumor bearing area, and curettage. The pathologic diagnosis was that of degenerating chondromyxoma. As usual the wound healed per primam.

The patient again remained symptom free for two and one half years, when, because of pain and roentgenographic evidence of a recurrence, it was decided that a segmental resection of the mid portion of the humerus was indicated. The fourth operation, performed on Jan. 18, 1936, consisted of resection of the middle third of the humerus with substitution of a massive tibial transplant for the defect. Following the operation, splenic extract was administered orally. The arm was immobilized with plaster shoulder splint,



Fig. 2.—A. Central chondroma of humerus following three failures to control by curettage lesion of border line malignancy. B. Appearance immediately after segmental resection and substitution of massive tibial transplant inserted at either end. C. Appearance eighteen months after operation. Ten years later the patient has excellent function, pursues former occupation as typist, and is free from any evidence of disease.

changed occasionally, for the next seven months. Thereafter physiotherapy was instituted and a special brace was made to support the limb. Roentgenograms revealed solid union of the transplant to the upper and lower portions.

One year after the fourth operation the patient returned to work as a typist and she has worked steadily for the past ten years. There has been no further return of the disease (see Fig. 2).

CASE 2—P. B., a man aged 29 years, was admitted to Memorial Hospital on Oct. 15, 1940, with a history of having sustained a crushing injury to the tip of the right thumb four years previously. The pain, swelling, and ecchymosis subsided but the thumb remained enlarged. Six weeks prior to admission he struck the tip of the same thumb



Fig. 3—Chondroma of mixed type. The tumor is partly central partly osteochondroma. The patient was a soldier and had remarkably little impairment of function. The symptoms though of long duration were mild.

with

and the tumor

Pathologic diagnosis was that of central chondromyxoma.

Roentgenographic examination on Feb. 11, 1941, revealed a practically normal contour of the thumb, no pain or disability, and healing. The patient was last seen five and one-half years after the operation, the anatomic and functional result had remained excellent.

CASE 3—N. L., a 71 year old man, was first seen at Memorial Hospital on March 3, 1943. He gave a history of pain and disability on flexion of the right knee over a period of five months. Six weeks prior to admission he had noticed a swelling on the anterior aspect of the lower third of the right thigh. Roentgenographic examination made else

... of the terminal phalanx consisted of curettage and healed per primam.

where showed what was diagnosed as metastatic carcinoma. Physical examination revealed a firm nontender mass measuring 18 cm situated on the anterior aspect of the lower third of the right thigh. Flexion was impaired beyond 80 degrees.

A review of the submitted roentgenograms disclosed a large irregular area of bone destruction in the lower end of the shaft of the left femur above the condyles indicating a primary bone tumor apparently medullary in origin.

An aspiration biopsy was done on March 11 1943 and the report was some type of cartilaginous tumor—the material largely cartilage and with almost no cells. Following a second aspiration biopsy on March 24 1943 the report was chondroma and a third aspiration on March 31 1943 was reported as fully malignant osteogenic sarcoma.

Roentgen therapy was instituted on March 15 1943 (before the diagnosis of sarcoma was established). A total of 1500 r at 250 kv and 1.0 cm target skin distance was given to each of two portals 24 by 15 in. On April 17 1943 a high thigh amputation was performed.



Fig. 4.—Extensive central chondroma. The patient was an adult colored man. This case was considered malignant on clinical and roentgenographic grounds and an amputation was performed. Its extent precluded a resection or a curettage. Tumors such as this have definite malignant potentialities. Patient was well nine years later.

and the pathologist reported *osteogenic sarcoma* on basis of an oil central chondroma. The patient made an *uneventful recovery*. The diabetes which was discovered preoperatively was well controlled. Pulmonary metastasis developed and he died eight months after the operation.

BENIGN CHONDROBLASTOMA

Benign chondroblastoma (Codman's epiphyseal chondromatous giant cell tumor) remained a confusing entity for years prior to its description by Codman, the founder and first registrar of the Bone Sarcoma Registry. He recognized it as a benign lesion and was aware of its cartilaginous nature but believed it belonged in the giant cell tumor group.



Fig. 7.—Chondroma of femur. The patient, a young adult man, had a fifteen year history of mild pain. Despite a lack of radiologic confirmation the roentgenographic appearance is typical of chondroma.

We have long felt that it is not a giant cell tumor and that it belongs properly with the tumors of cartilaginous origin. Jaffe and Lichtenstein considered it to be distinct from giant cell tumor and not even a variant of it. They termed it a benign chondroblastoma. Little would be gained here by repeating the description and arguments; those interested should read the original article.

We are presenting eight cases of this condition observed in the bone tumor department of Memorial Hospital prior to Jan. 1, 1946.

Age and Sex—As shown in Table IV, four of our cases were in the age group from 11 to 20 years, while all of the cases of Jaffe and Lichtenstein were in this decade.

Again, in contrast to their series which were all males, ours showed the sexes to be equally divided; that is, four males and four females.

Location of Bone Involvement—Codman's original description covered a small number of cases all involving the upper end of the humerus; however

TABLE IV

AGE (YEARS)	NUMBER OF CASES
Under 11	1
11 to 20	4
21 to 30	1
31 to 40	1
41 to 50	0
51 to 60	1
Total	8

cases were soon reported showing the lesion to be by no means confined to that locality. Jaffe and Lichtenstein considered that they probably began in the epiphysis and involve the metaphysis secondarily. Our experience supports this assumption.

TABLE V

BONE INVOLVED	NUMBER OF CASES
Femur	1
Humerus	2
Tibia	1
Metacarpal	1
Astragalus	1
Total	6

Clinical Manifestations—Pain and swelling at the site of the lesion is the usual complaint. Trauma has not been shown to be of etiologic importance although an injury to the part might well attract the patient's attention to it. Only two of our eight patients gave a history of antecedent injury and in neither did there seem to be any convincing evidence of a causal relationship. The correct diagnosis was arrived at only once prior to receipt of the pathologist's report.

Pathology—According to Jaffe and Lichtenstein the tumor is derived from cartilage germ cells or chondroblasts. Calcification of the necrotic matrix in irregular areas is a distinctive feature of the disease but this has not been present in recognizable degree in some of our cases. The giant cell elements responsible in the past for the inclusion of this neoplasm among the giant cell tumors are multinuclear macrophages. They may appear in the hyaline chondroid tissue in areas of hemorrhage and around vascular sinuses.

Treatment—Perhaps because of their more primitive cellular pathology these tumors are somewhat radiosensitive certainly more so than are ordinary chondromas. Hence there is a possibility that roentgen therapy may be an entirely acceptable method of treatment. However since an operation is usually necessary to establish the diagnosis and since conservative surgical measures have proved satisfactory we regard surgery as the method of choice. One may deal with these tumors much as with the giant cell tumor or the central chondroma if the removal is thorough the results are satisfactory.

TABLE VI

METHOD EMPLOYED	NUMBER OF CASES
Roentgen rays only	3
Surgery only (curettage)	5
Total	8

CASE 4.—T T, a girl 13 years of age was admitted to Memorial Hospital on Nov. 14, 1915, complaining of persistent pain in the medial side of the left knee of six months duration. The pain was more intense at night or when walking or standing for long periods. Two months after the onset she was told that it was a sprain and was treated with warm compresses. Three months after the onset roentgenograms were taken which were said to be negative. Finally a roentgenogram was made which showed an area of



Fig. 6.—Dyschondrodysplasia. At the site of the profound structural changes in the upper femoral region a secondary chondrosarcomatous degeneration has developed. The long bones of the entire lower extremity showed the characteristic features of hereditary deforming dyschondrodysplasia. The condition was inoperable and caused the patient's death.

decalcification in the medial condyle of the left femur. Physical examination on admission disclosed practically nothing more than a slight degree of tenderness on the medial aspect of the left femur in the condylar region and a 1 cm increase in circumference at this level as compared with the normal side. Roentgenograms revealed a cystic area of bone destruction in the medial condyle of the femur measuring about three quarters inch in diameter. Roentgenograms made over a period of several months showed a slight in-



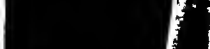
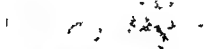
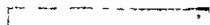
Fig 7



Fig 8

Fig 7—Fibrous dysplasia the appearance is suggestive of central chondroma.
 Fig 8—Benign chondroblastoma curettage was successfully employed.

CASE 4—T T a girl 17 years of age was admitted to Memorial Hospital on Nov 14 1945 complaining of persistent pain in the medial side of the left knee of six months duration. The pain was more intense at night or when walking or standing for long periods. Two months after the onset she was told that it was a sprain and was treated with warm compresses. Three months after the onset roentgenograms were taken which were said to be negative. Finally a roentgenogram was made which showed an area of



normal. There was no alteration in the knee joint function, but there was some atrophy of the muscles of this extremity. The roentgenographic appearance of the lesion in the upper end of the right tibia was cystlike and it was diagnosed by the roentgenologist of Memorial Hospital as a Codman's tumor. Operation on Oct. 21, 1943, consisted of curettage and insertion of a tibial bone graft from the opposite tibia. The tumor was found to lay directly beneath the periosteum at one point and it was unnecessary to divide the bony cortex in order to gain access to it.

Pathologic report was atypical case of Codman's epiphyseal chondromatous giant cell tumor (benign chondroblastoma of bone).

This patient was followed over a period of more than two and one half years, meanwhile successive roentgenograms showed that the lesion healed satisfactorily and there was no evidence of a recurrence.

SUMMARY

1 Records of twenty two central chondromas and eight chondroblastomas have been studied and conclusions have been presented.

2 The long bones are predominantly involved in both conditions, both are essentially diseases of youth and early adult life.

3 Pain and swelling are the most frequent initial complaints.

4 Chondroblastoma more closely resembles giant cell tumor than does central chondroma. At times chondroblastoma presents roentgen evidence suggestive of a malignant bone sarcoma.

5 Surgical measures are applicable to both conditions. Roentgen therapy may be successful in chondroblastoma but it is not of value in central chondroma.

6 Chondroblastoma is neither a variant of giant cell tumor nor is it confined to the upper humerus.

7 Cartilage tumors may remain benign but they may also become malignant, metastasize, and cause death.

8 Chondroma and chondroblastoma should never be regarded as inconsequential conditions that can safely be ignored. Whenever possible they should be removed surgically.

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crease in the size of this area. According to the roentgenologist a diagnosis of chondromatous giant cell tumor was the more likely one.

On Nov. 29, 1947, an operation was performed as follows: through a transverse incision a window was made in the outer shell of the medial condyle measuring 1 cm., giving access to the cavity which was immediately curetted. It was then swilled with zinc chloride and flushed with normal saline solution following which it was filled with chips taken from the window, the wound was closed in layers without drainage. Primary wound healing took place. The pathologist reported Codman's chondromatous giant cell tumor (chondroblastoma). The postoperative course was uneventful. The patient was last seen on July 16, 1948, at which time she was living a completely normal existence. The wound was well healed and movements of the knee were complete.

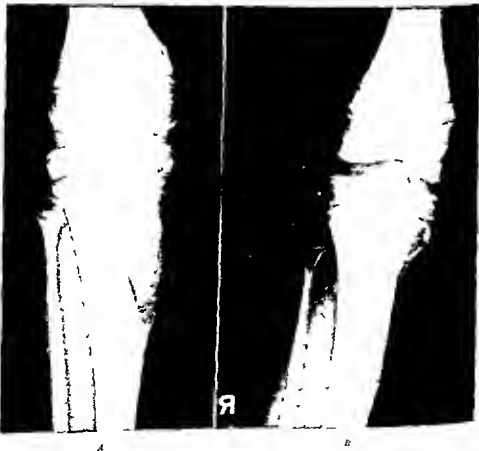


FIG. 9.—Benign chondroblastoma (Codman's epithelioid chondromatous giant cell tumor). A: The extent of the lesion and its sharp limitation at the epiphyseal line. B: A bone regeneration and satisfactory healing following curettage of the involved area.

CASE 3.—B. M., a 9-year-old girl, was admitted to Memorial Hospital on Oct. 2, 1945. The chief complaint was pain in the upper end of the right leg, of eight months' duration. Two months after its onset a swelling was noticed which persisted afterward. The child was rather poorly nourished, somewhat emaciated, and physical examination did not reveal anything significant beyond that of the local condition. In the upper end of the right tibia was a tender, fusiform swelling measuring 8 by 6 cm. the skin over which was

normal. There was no alteration in the knee joint function but there was some atrophy of the muscles of this extremity. The roentgenographic appearance of the lesion in the upper end of the right tibia was cystlike and it was diagnosed by the roentgenologist of Memorial Hospital as a Codman's tumor. Operation on Oct 21 1943 consisted of curettage and insertion of a tibial bone graft from the opposite tibia. The tumor was found to lay directly beneath the periosteum at one point and it was unnecessary to divide the bony cortex in order to gain access to it.

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This patient was followed over a period of more than two and one half years meanwhile successive roentgenograms showed that the lesion healed satisfactorily and there was no evidence of a recurrence.

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CLINICAL EVALUATION OF BOVINE SERUM ALBUMIN AS A BLOOD SUBSTITUTE

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WORLD WAR II accentuated the need for a satisfactory blood substitute. This need, however, is not entirely related to military surgery, for the use of whole blood, plasma, and serum in civilian practice has become much more extensive since the principles of the prevention and treatment of shock and contracted protein stores have become better appreciated.

Although human blood plasma, and serum are, on general physiologic grounds, the most ideal transfusion fluids, still the difficulty in obtaining and storing them in large quantities makes them far from ideal from a practical point of view. A blood substitute derived from bovine blood provided it were satisfactory in other respects because of its practically unlimited source would thus obviate all difficulties associated with the procurement from a human source. Also, Cohn¹⁰ felt "that the most effective materials for transfusion will often prove to be concentrates from blood—including concentrated red or white cells—of the components with specific physiological functions which are deficient in any given clinical condition."

The use of bovine plasma and serum has not found wide use for it was felt that they were toxic to man. A review of the literature however reveals only the scarcity of factual data on this point. Shortell, Cotting, and Leary¹ reported, in 1916, on the use of bovine plasma principally in the topical application to wounds. Penna and associates² in 1917 used bovine serum intravenously and intramuscularly in the treatment of anthrax with some good results. In 1921 Krause and co-workers³ injected 198 children intravenously and intramuscularly with diphtheria and tetanus antitoxin prepared from cows. The amounts injected varied from 5 to 50 cc and the incidence of serum sickness was 6 per cent. Approximately eight years ago exploration of the thesis that bovine plasma might serve as a blood substitute in the treatment of hemorrhagic shock and other states was begun in this surgical clinic.^{4, 5} In a series of papers it was shown that bovine plasma could be given intravenously to man with relative safety, although the incidence of immediate reactions was approximately 50 per cent and that of delayed reactions between 47 and 60 per cent.

The work described in this paper was done under a contract recommended by the Committee on Medical Research from the Office of Scientific Research and Development and the

d for Surgical Research and a grant from

By adsorbing bovine serum on human red blood cells the incidence of immediate reactions was reduced to approximately 24.5 per cent but the number of delayed reactions was not materially lessened.

In an effort to determine the source of the reactions Kremen, Taylor, and Hall⁶ fractionated whole bovine plasma by ammonium sulfate precipitation and skin tested individuals to these fractions as well as to whole bovine plasma. They found that albumin caused the least number of positive reactions, the globulin was intermediate and the whole plasma caused the largest number of positive reactions as well as those of greatest magnitude.

At the request of Dr. W. Cannon* and Dr. D. Edsall† Cohn and co-workers undertook an investigation to determine whether plasma of animals could be made safe for human transfusion. Their earliest attempts at fractionation of bovine plasma were by the ammonium sulfate precipitation method⁷ but materials so obtained were used only to correlate the salting out procedures with other methods which were being investigated and were not intended for clinical testing. Cohn and his co-workers recognized that the ammonium sulfate precipitation method which had been in use for almost a century and to the understanding of which they had so largely contributed⁷ would prove to be inadequate for the preparation in large amounts of proteins purified, concentrated and rendered safe for intravenous injection. New methods for the fractionation of plasma in alcohol-water mixtures at low temperatures and controlled pH, protein and salt concentration were developed by the Harvard group during the spring and summer of 1940.^{8, 9} Highly purified bovine serum albumin preparations so obtained proved similar to human serum albumin in such physicochemical properties as molecular size and shape and osmotic efficiency but differed slightly from human serum albumin in solubility and in amino acid composition and could be readily differentiated by immunologic procedures such as precipitation reaction. Janeway and Beeson¹⁰ injected this highly purified bovine serum albumin fraction into sixteen human subjects with three very mild immediate reactions and only two delayed serum sickness reactions. In June 1941 Cohn and Hughes Jr. were for the first time able to accomplish crystallization of bovine serum albumin.¹¹ Keys, Taylor, and Savage¹² stated in a letter that they had separated the albumin fractions from bovine plasma by precipitation with ammonium sulfate, ammonium phosphate and alcohol and found that bovine serum albumin gave far less reactions than did whole bovine plasma when injected into human beings.

Other investigators also felt that the antigenicity of bovine plasma or serum resided primarily with the globulin fraction and attempted to separate off the albumin portion. Davis, Eaton and Williamson¹³ injected thirteen patients with bovine serum albumin precipitated with saturated ammonium sulfate solutions without immediate reactions.

Lewis and Edwards¹⁴ attempted to remove the antigenicity of whole bovine plasma by desiccation. The former treated bovine plasma with 0.5 N so-

*Then Chairman of the Committee on Blood and Transfusions of the National Research Council.

†Then Chairman of the Medical Advisory Committee of the American Red Cross.

dium hydroxide at 37° C for one hour, the latter heated bovine serum to 57° C and prevented coagulation of the serum proteins by the addition of 0.2 per cent liquor formaldehyle and 0.2 per cent 0.880 N ammonia. Edwards¹⁷ injected twenty six individuals with only three immediate reactions and no delayed reactions.

MATERIALS AND METHODS

The bovine serum albumin solutions used were supplied by Cohn and Hughes Jr. of the Harvard Medical School and Dr J. D. Porsche* and Dr J. B. Lesh*. Those made available to us by Porsche and Lesh were prepared and tested in collaboration with the Harvard group. During the initial testing period (Series A & 1) the character of the preparation was continually changing as improvements in the method of preparations were found. However the later preparations as tested in Series B, C, D represented a chemically uniform product of bovine serum albumin which had been crystallized four times from ethanol-water mixtures of controlled pH, temperature and ionic strength.^{9, 10, 12}

In series C were included preparations of respectively first and second crops of crystals. However as statistical evaluation showed no clinical difference only the summary of the total experience is here reported.

All preparations in Series B, C, D were received as sterile ampules containing 20 Gm. of albumin dissolved in 100 cc. of saline solution and neutralized to pH 6.6. A preservative (merthiolate) which had been used in Series A was discontinued in the later series because of fear it might enhance the antigenicity of the preparations. Bacteriologic studies failed to reveal contaminating bacteria in any of these preparations. All preparations were of proved low globulin content and excepting Series A were of high stability. They were free of pyrogens by rabbit thermal test and were nontoxic to guinea pigs. Analysis of the more pertinent physical and chemical properties of crystallized bovine serum albumin at the Harvard Plasma Fractionation Laboratory revealed the following: globulin (by precipitin test) 0.05 per cent, carbohydrate (orcinol test) 0.1 per cent, nitrogen (macro Kjeldahl) 16.0 per cent, molecular weight (from osmotic pressure) 69,000.

The patients used in this study were from the surgical services of the University Hospitals. In the earlier periods of this investigation only patients with advanced malignancies were employed but as it became apparent that the albumin solutions could be given with no fear of immediate reaction only individuals who were in good physical condition, afebrile and who had no history of allergy were injected. Prior to administration the blood pressure, respirations and temperature of the patient were obtained. In the earlier parts of this study a skin test (0.05 cc. of 1/10 dilution of bovine serum albumin solution intracutaneously 125 mg.) was applied but for reasons to be given this practice was abandoned later. Ten cubic centimeters of blood were drawn into a nonoxalate tube and set aside in an icebox for several days after which the serum was drawn off in a suitable container, labeled and kept. This was done so that if a delayed reaction occurred immunologic differences could be determined between the patient's serum prior to injection and during and following

*Of the Armour and Company Laboratories, Chicago, Ill.

the period of delayed serum sickness. A syringe containing 5 cc of $\frac{1}{1000}$ adrenalin hydrochloride was kept at the bedside while the patient was being studied, so that it could be given immediately if any untoward reactions were encountered. The unit of bovine serum albumin employed was 25 Gm. It was diluted to 200 cc with normal saline solution, given intravenously by the gravity drip method at a height of about four feet and at a rate such that the injection took between twenty to forty minutes. The patient's temperature, pulse, respirations, and blood pressure were checked every fifteen minutes for the first hour and then every one half hour for three hours after the transfusion. The patients were then checked at intervals of three and six weeks after the injection both by questionnaire and return visit to the clinic. If no untoward reactions were detected by these means the patients were considered not to have developed delayed serum sickness reaction. If the patient, however, developed a reaction he was hospitalized and complete blood and urine analyses as well as electrocardiogram, capillary fragility, prothrombin levels, and phenolsulfonphthalein kidney function tests were obtained.

Samples of blood were drawn whenever possible at the beginning, at the height of, and one month after the subsidence of the delayed serum sickness. These along with the preinjection sample were forwarded to Janeway of The Children's Hospital at Boston for immunologic studies.

OBSERVATIONS

For reasons stated previously the patients injected were placed in four series. Series A (patients injected from October 1941, to February, 1943), Series B (patients injected from April 1943 to July 1943), Series C (patients injected from September, 1943, to September, 1945), and Series D, covering the same time interval as Series C but consisting of patients who had one previous injection of bovine serum albumin and subsequently were reinjected.

Series A (October 1941, to February 1943).—In all 82 patients received 135 injections with eight immediate reactions (9.7 per cent) and nine delayed reactions (10.8 per cent). (See Table I.)

The immediate reactions were of two main types (1) anaphylactoid, characterized by dyspnea, urticaria, cyanosis and a fall in blood pressure and (2)

TABLE I. INCIDENCE OF IMMEDIATE AND DELAYED REACTIONS

SERIES	NO OF PATIENTS INJECTED	NO OF INJECTIONS	IMMEDIATE REACTIONS		IMMEDIATE REACTIONS OF PATIENTS INJECTED		DELAYED REACTIONS OF PATIENTS INJECTED	
			FEVER GENIC	ANAPHYLACTOID	TOTAL NO	PERCENTAGE	TOTAL NO	PERCENTAGE
A	42	135	8*	2	8	9.7	9	10.8
B	57	60	0	0	0	0	7	12.3
C	232†	232†	34	04	3	13	20‡	8.5
D	39	42	0	1	1	2.6	2	5.2
Total	410	469	9	3	11	2.9	38	9.2

*In one case

†Bovine

‡Bovine

not incl

preparation AMB, and 29 injections with

tabling

... bovine serum albumin preparation AMB,

†Two moderately severe delayed reactions following the injection of bovine serum albumin preparation AMB, not included

pyrogenic, characterized by chills and fever. The reactions were classified as mild, moderate, and severe. In the anaphylactoid group the mild reactions exhibited urticaria alone, the moderate reactions dyspnea, cyanosis and urticaria, and the severe reactions, a shocklike fall in blood pressure. In the pyrogenic group, the mild reactions were characterized by slight chills and fever ranging up to 100° F., the moderate reactions by chills of moderate severity and fever not exceeding 103° F., and the severe reactions by severe chills and a temperature over 103° F. On this basis (Table II) there were two mild, five moderate, and one severe reaction. The latter was probably not due to the bovine albumin, for a sporeformer was cultured from the fluids administered indicating contamination of the solution or rubber tubing.

TABLE II SEVERITY OF IMMEDIATE AND DELAYED REACTIONS

SERIES	IMMEDIATE REACTIONS						DELAYED REACTIONS		
	PYROGENIC			ANAPHYLACTOID			MILD	MODERATE	SEVERE
	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE			
A	1	4	1*	1	1	0	3	6	0
B	0	0	0	0	0	0	1	5	1
C	0	0	1†	0	0	0‡	4	13§	1
D	0	0	0	1	0	0	1	1	0
Total	1	4	1	2	1	0	9	21	2

*Sporeform cultured from fluids

†Probably due to pyrogens in diluents or rubber tubing

‡One severe anaphylactoid reaction followed the injection of bovine serum albumin preparation AMB; not included

§An additional two delayed reactions of moderate severity followed the injection of bovine serum albumin preparation AMB.

The delayed reactions began usually between fourteen and twenty-one days after injection and were characterized by arthralgia, myalgia, and urticaria. The patients with more severe reactions had, in addition, vomiting, diarrhea and generalized petechial rash. In this series, three mild and six moderately severe reactions were noted (Table II). There were no severe reactions. The incidence and type of reaction with each of the bovine serum albumin preparations utilized are given in Table III. Skin tests were positive in six individuals (73 per cent of the patients injected) as indicated by the presence of erythema.

TABLE III INCIDENCE OF REACTIONS SERIES A

PREP ARATION	NO OF PATIENTS INJECTED	NO OF INJECTIONS	IMMEDIATE REACTIONS		PATIENTS INJECTED		DELAYED REAC- TIONS OF PA- TIENTS INJECTED	
			PYRO- GENIC	ANAPHY- LACTOID	TOTAL NO	PER- CENTAGE	TOTAL NO	PER CENTAGE
Alb ₁	7	7	0	1	1	14.2	2	28.4
CB ₁	3	3	1	0	1	33.3	0	0.0
CB ₂	4	4	0	0	0	0.0	0	0.0
CB ₃	4	4	0	0	0	0.0	1	16.6
ACB ₁	4	4	0	0	0	0.0	0	0.0
ACB ₂	7	9	4	0	4	57.1	2	28.6
ACB ₃	2	2	1	0	1	46	1	46
ACB ₄	2	7	0	0	0	0.0	0	0.0
ACB ₅	2	4	1	0	1	55.5	3	16.6
ACB ₆	18	43	0	0	0	0.0	0	0.0
ACB ₇	7	24	0	0	0	0.0	0	0.0
CB ₄	2	2	0	0	0	0.0	0	0.0
Total	82	175	7	1	8	9.7	9	10.8

and wheal formation. In an additional four the test was equivocal for erythema without wheal formation occurring at the test site. Of the six patients with positive skin tests, five were injected with bovine serum albumin solutions without reactions. Of the six patients developing pyrogenic reactions one patient had a positive skin test. Of the two patients who developed immediate anaphylactoid reactions one had a negative skin test and the other had a questionable positive test in that only erythema occurred at the skin injection site. In view of this poor correlation between the negativity and positivity of the skin test with the subsequent development or failure to develop immediate reactions it was felt that skin testing was of little help in determining likely reactors.

In this series forty-four patients received more than one injection. Thirty-four patients received two injections, five patients received three injections, one patient received four injections, and one patient received six injections. The time interval between injections varied from twenty-four hours to approximately eighteen months. In all but six the time interval however exceeded twenty-seven days. There were no immediate reactions on repeated injections and only four delayed reactions (8.1 per cent). Of these four one patient had a second injection ten days following the first, the remaining three had the second injection at 78, 314, and 81 days respectively following the original injection.

Ten patients had received bovine plasma from one to two years previously and six had developed both immediate and delayed reactions. However, not one of these patients developed either immediate or delayed reactions subsequent to the injection of crystallized bovine serum albumin solutions.

Series B (April 1943 to July 1943)—In all fifty-seven patients received sixty injections with no immediate reactions and seven delayed reactions (12.3 per cent) (Table I). Of the seven reactions, one was mild, five were moderately severe and one was severe (Table II). The incidence and type of reaction with each of the bovine serum albumin preparation used is given in Table IV.

Skin tests were applied to all patients in this series with the exception of three. All of the skin tests were negative.

Series C* (September 1943 to September 1946)—There were 232 new injections into an equal number of patients with three immediate pyrogenic reactions (1.3 per cent) and twenty delayed reactions (8.6 per cent) (Table I).

All of the pyrogenic reactions may have been due to pyrogens within the rubber tubing or our own diluents, for they occurred when there was a large number of similar pyrogenic reactions attending the administration of simple glu-

*In Series C, eight patients reacted with immediate severe anaphylactoid serum albumin.

of formaldehyde 1 to the protein like AMB, its contraindications were very not been

TABLE IV. INCIDENCE OF REACTIONS, SERIES D

PREP ARATION	NO OF PATIENTS INJECTED	NO OF INJECTIONS	IMMEDIATE REACTIONS		PATIENTS INJECTED		DELAYED REACTIONS OF PATIENTS INJECTED	
			PYRO GENIC	ANAPHY LACTOID	TOTAL NO	PER CENTAGE	TOTAL NO	PER CENTAGE
CB ₁	20	20	0	0	0	0.0	1	4.0
ACB ₁	25	30	0	0	0	0.0	5	17.9
ACB ₂	4	4	0	0	0	0.0	1	2.5
Total	57	60	0	0	0	0.0	7	12.3

cose and saline solutions. If these were excluded, the over all incidence of immediate reactions would thus have been 0 per cent.

Table II indicates that the majority of delayed reactions were of either mild or moderate severity. In only one instance was the reaction particularly severe. Table V lists the incidence and type of reaction with each of the bovine serum albumin preparations used.

TABLE V. INCIDENCE OF REACTION, SERIES C

							DELAYED REACTIONS OF PATIENTS INJECTED	
							AL	PER CENTAGE
								6.3
								8.5
								12.5
ACB ₁ , H ₂	0	0	0	0	0.0	0	0.0	
ACB ₂	10	0	0	0	0.0	1	8.3	
ACB ₃	12	0	0	0	0.0	2	8.0	
ACB ₄	25	0	0	0	0.0	3	5.2	
ACB ₅	59	0	0	0	0.0	4	12.2	
ACB ₆	32	0	0	0	0.0	2	42.9	
ACB ₇	7	0	0	0	0.0			
Total	232	3	0	3	1.3	21	9.6	

X. Probably due to pyrogens within the rubber tubing or diluents.

Series D (Reinjection series September 1944, to September 1945)—Thirty nine patients received 42 injections with one immediate reaction (2.6 per cent) and two delayed reactions (5.2 per cent) (Table I). The time interval between injections varied from 10 to 807 days.

TABLE VI. INCIDENCE OF REACTIONS, SERIES D

PREP ARATION	NO OF PATIENTS INJECTED	NO OF INJECTIONS			PATIENTS INJECTED		DELAYED REACTIONS OF PATIENTS INJECTED	
							AL	PER CENTAGE
	18	18						5.6
ACB ₁	7	7	0	0	0	0.0	0	0.0
ACB ₂	5	5	0	0	0	0.0	0	0.0
ACB ₃	9	12	0	1	1	11.1	1	11.1
ACB ₄			0	1	1	2.6	2	5.2
Total	39	42						

The immediate reaction was of mild severity and occurred in a patient (V B, U H No 730470) who had developed delayed reactions to two previous injections of bovine serum albumin preparations.

Of the delayed reactions, one was mild and one of moderate severity (Table II). Both of the patients had developed serum sickness on previous injections of bovine serum albumin solutions. The incidence and type of reaction with each of the bovine serum albumin preparations injected are given in Table VI.

That a previous reaction either immediate or delayed, following the injection of bovine serum albumin, is not always repeated on subsequent injection is evidenced by the circumstance that two patients who had had immediate reactions and three patients who had delayed serum sickness following previous injections on this occasion did not experience further difficulty when injected.

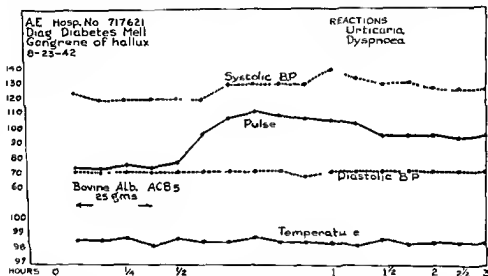


Fig 1—Pyrogenic reaction following the administration of bovine serum albumin preparation ACB5.

A typical example of a moderately severe immediate reaction seen in the study is that of A F U H No 717621 No 40 Series A, a white, 62 year old man, with diabetic gangrene of the left great toe who received 25 Gm of bovine serum albumin preparation ACB5 in ten minutes on Aug 23, 1942. He then developed urticaria, dyspnea, hoarseness, and edema of the eyelids. There was a moderate elevation of the pulse rate but no change in temperature, respiration and blood pressure (Fig 1). The manifestations were readily controlled by the administration of 0.5 cc of $\frac{1}{1000}$ adrenalin hydrochloride subcutaneously.

The most severe delayed reaction occurred in the instance of M E, U H No 740179, No 38 Series C, a white 19 year old man, who was admitted to the hospital for a traumatic laceration of the right ulnar and median nerves. On May 16, 1944, he received 25 Gm of bovine serum albumin preparation ACB56 without reaction. On May 30 1944 (twelve days later), he noted headache,

anorexia, and cervical adenopathy. On the following day, he developed arthralgia, myalgia, chills, fever, and maculopapular rash on the feet and legs. On June 5, 1944, he developed a purpuric rash over the back and a bloody diarrhea. Blood pressure fell from 100/90 mm Hg to 86/60 and he was given 500 cc of whole blood with elevation of the blood pressure to 110/70 mm Hg. The general condition remained unchanged until June 11, 1944, when all signs and symptoms apart from arthralgia and a low grade fever subsided.

He was given 1 Gm of procaine in 500 cc of saline solution intravenously on June 14, 1944, with prompt disappearance of the fever and subsidence of the arthralgia. This response to procaine led to its use in all subsequent cases of delayed serum sickness with excellent results.¹⁸ It is quite possible that if we had used it earlier in this patient the severity and duration of the serum sickness might have been lessened materially.

Summary—In all 410 patients received 469 injections with twelve immediate reactions (29 per cent) and 38 delayed reactions (9.2 per cent) (Table I). Of the immediate reactions, three were mild, five moderately severe, and four severe. Of the delayed reactions, nine were mild, twenty seven moderately severe and two severe (Table II).

When one compares the incidence and severity of both immediate and delayed reactions in this study with those published by Kremen and associates¹⁴ with bovine plasma it can readily be appreciated that real progress has been made by separating out and purifying the albumin fraction, immediate reactions virtually have been eliminated and the incidence of delayed serum sickness has been reduced considerably.

At present, bovine serum albumin solutions can be given with no fear of immediate reaction beyond the incidence rate of reaction attending the administration of whole blood.¹⁹ It is only fair to add however, that delayed antigenic reactions of bovine serum albumin are somewhat more disturbing. Also the severe anaphylactoid reactions that followed the administration of bovine serum, plasma, and the earlier albumin fractions separated by precipitation with ammonium sulfate have been eliminated entirely in the later preparations of Cohn and Hughes, Jr. One further point of interest and great practical importance is that the incidence of immediate reactions is no greater in the re-injection series than in the initial injection series.

The incidence of immediate reactions in Series B, C, and D can be considered to be 0 per cent approximately. As explained previously three of the reactions in Series C might well have been due to contamination of the rubber tubing or our own diluents for they occurred at a time when many reactions appeared throughout the hospital even following the administration of glucose and saline solutions.

In contrast to this marked and progressive decrease in the incidence of immediate reactions there has not been a continual decrease in the incidence of delayed reactions. Following the marked initial drop attending the utilization of the purified albumin fraction as contrasted to whole bovine plasma and serum the percentage of delayed reactions has remained fairly constant at 5 to

10 per cent in all of the series. It should again be emphasized that the incidence of delayed reactions in the reinjection series is no higher than in the initial injection series.

Two major problems therefore present themselves. First the elimination of the delayed reactions and second the detection of possible reactors.

The elimination of delayed reactions by still further purification of bovine serum albumin seems hardly likely for some of the bovine serum albumin preparations supplied to us by Cohn and Hughes, Jr. have had as little as 0.05 Gm per cent of globulin and yet delayed reactions attended their use. Desperation according to the method of Edwards¹⁶ also has failed to eliminate both immediate and delayed reactions. It is to be hoped that someone will come forward with a plan which will eliminate the antigenic factor in bovine serum albumin.

The methods used to detect possible reactors have consisted of skin testing and close questioning of the individuals for allergies prior to the administration of bovine serum albumin. Both of these methods have been unsuccessful. Delayed reactions occurred frequently in the absence of a positive skin test and despite a negative history of hypersensitivity. Conversely patients with a positive skin test or history of allergy did not develop either immediate or delayed reactions. However it should be noted that no strongly positive skin tests were encountered and it is possible that only very strongly positive skin tests (wide flare, large wheal, itching and pseudopods) have real significance.²⁰

INTRAVENOUS PROCaine ABORTS SERUM SICKNESS

Procaine given intravenously was an extremely effective antidote for serum sickness.¹⁸ Sixteen patients with delayed serum sickness were given 2 Gm. of procaine diluted to 500 cc. with normal saline over a period of two hours. Ten individuals obtained immediate and complete relief after one or more injections. An additional four obtained only temporary or partial relief and two were not benefited at all.

Its exact mode of action is not clear but the following hypotheses have been postulated: (a) direct action on the cells, (b) antihistamine action, (c) anti-acetylcholin action and (d) adrenalin potentiating action.

PERIARTERITIS NODOSA AND PANCREATITIS NOT OBSERVED

Barley and Hawn²¹ have been able to demonstrate the presence of periarteritis nodosa and pancreatitis in rabbits sensitized to bovine serum albumin. In this study it was possible to check the post mortem findings in seven patients who had received bovine serum albumin but had died of other causes. Two of these patients had had serum sickness. The time interval between the last injection of bovine serum albumin and the autopsy varied from two days to eighteen months in these patients. There was no pancreatitis and in no instance were evidences of periarteritis nodosa observed either grossly or microscopically in the following organs: brain, lungs, skin, spleen, heart, esophagus, stomach, duodenum, small and large bowels, liver, pleura, kidneys, gall bladder, urinary bladder, prostate, testes, ovary, uterus, iliopectineal tubes, aorta, vertebrae and renal psoas muscle and diaphragm.

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PERIARTERITIS NODOSA AND PANCARDITIS NOT OBSERVED

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EFFICACY OF BOVINE SERUM ALBUMIN SOLUTIONS AS A BLOOD SUBSTITUTE

Since most of the surgery in the surgical division of the University Hospitals is of an elective nature, few cases were available to study the effectiveness of bovine serum albumin solutions in the treatment of shock. In the earlier phases of the work, three patients who were in shock were available and were studied. Two patients who underwent major surgical procedures and to whom bovine serum albumin was given to determine its value in the prevention of the onset of shock were studied. As this investigation progressed it became apparent that the prime phase of importance was to determine the safety of administration of bovine serum albumin solutions and it was felt that multiple large injections of bovine serum albumin solutions should not be given until more definite data on its relative safety in administration were available. Because of this the study of the efficacy of bovine serum albumin in prevention and treatment of shock was not pursued.

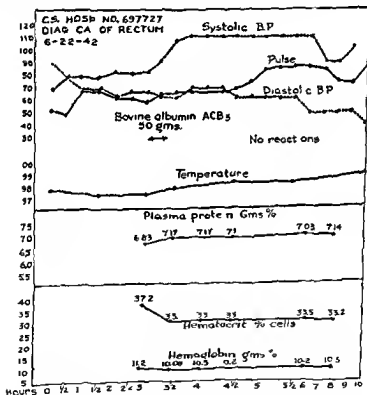


Fig. 1.—Efficacy of bovine serum albumin in the treatment of shock.

BOVINE SERUM ALBUMIN SOLUTIONS IN THE TREATMENT OF SHOCK

CASE 1 (U H No 697727)—C S., a white man, was 64 years of age. Diagnosis of carcinoma of the rectum with extensive metastases was made. On June 20, 1942, he had bilateral cervical chordotomy for intractable pain secondary to metastases to the lumbar

spine and pelvis. The operation lasted from 3 30 to 5 30 P.M. Although the blood loss was not measured, it was thought not to be excessive. The blood pressure at the start of the operation was 158/74 mm Hg and the pulse 76 per minute. Toward the end of the operation the blood pressure fell to 90/60 mm Hg and the pulse was 82 per minute. During the operative procedure he received 1,000 cc of normal saline solution intravenously. For the first four hours after surgery the blood pressure ranged between 78/52 and 84/60 mm Hg and the pulse between 72 and 90 per minute. During this period he received 1,000 cc of 5 per cent glucose in normal saline solution intravenously and 1,000 cc of 5 per cent glucose in distilled water subcutaneously without appreciable effect on blood pressure or pulse rate. At 9 35 P.M. (approximately four hours after completion of the operation) he was given 50 Gm of bovine serum albumin solution ACB, diluted to 300 cc with normal saline solution in twenty minutes. The blood pressure began to rise almost immediately. At 10 P.M., it was 110/64 mm Hg, and it remained at about this level until 3 A.M., when observations were discontinued. Although there was little change in the pulse rate, there was a definite improvement in its quality. The hemoglobin (Sahli), hematocrit (Wintrobe tube 3,000 revolutions per minute for thirty minutes), and plasma proteins were taken immediately before the administration of the bovine serum albumin solution and at one half and hourly intervals thereafter. Definite evidence of rather marked hemodilution was noted following the use of the bovine serum albumin solution (Fig 2).

CASE 2 (U H No 673124) — R T, a white man, was 48 years of age. Diagnosis of chronic osteomyelitis of the left tibia was made. On March 3, 1942, he had a skin flap applied over a cutaneous sinus, secondary to chronic osteomyelitis of the left tibia. There was considerable bleeding (amount, however, was not measured) and the operation lasted three hours and fifteen minutes. During the first hour of operation, the blood pressure was consistently 170/90 mm Hg and the pulse 96 per minute. During the second hour of operation, the blood pressure fell to 140/70 mm Hg, and the pulse rose to 110 per minute. He was then given 500 cc whole blood with no change in blood pressure or pulse. In addition to the blood the patient received 500 cc normal saline solution intravenously during the operation. On returning to his bed in the surgical ward, the patient's blood pressure fell to 60/14 mm Hg and the pulse rose to 118 per minute. He was placed in steep Trendelenburg position but no parenteral fluids were given. During the next forty minutes the blood pressure rose gradually to 80/30 mm Hg, but the pulse remained between 100 and 110 per minute. He was then given 100 cc of bovine serum albumin solution CB₂ (25 Gm) undiluted over a period of fifteen minutes. Five minutes after the albumin solution had run in, the blood pressure rose to 100/60 mm Hg and the pulse slowed to 90 per minute. The blood pressure then was maintained adequately between 100/60 to 140/60 mm Hg until the patient regained full consciousness in two and one half hours. In this same interval the patient also received 500 cc of 5 per cent glucose in normal saline solution intravenously. Unfortunately, hemoglobin, hematocrit, and plasma protein values were not obtained.

CASE 3 (U H No 723323) — M K, a white woman, was 23 years of age. Diagnosis of compound fracture of the right tibia and lacerated tendons of the right leg was made. This patient was injured on Aug 17, 1942, approximately two hours before coming into the hospital. On admission, she was in acute pain and the skin was cold, moist, and pale. A tourniquet had been in place around the right leg for approximately one hour. The blood pressure, pulse and respiration were respectively 132/70 mm Hg, 90, and 24 per minute. Prior to surgery, she was given 100 cc (25 Gm.) of bovine serum albumin solution ACB, diluted to 200 cc with normal saline solution and during the operation for reduction of the fracture and repair of the tendons she was given an additional 25 Gm. In addition, she received 500 cc normal saline solution during surgery. The operation lasted two hours and fifteen minutes and apart from a temporary fall of blood pressure subsequent to the release of the tourniquet the blood pressure was uniformly maintained between 120/70 and 130/70 throughout and following the surgical procedure. The accompanying chart (Fig 3) also shows the fall in hemoglobin and hematocrit values indicating definite hemodilution.

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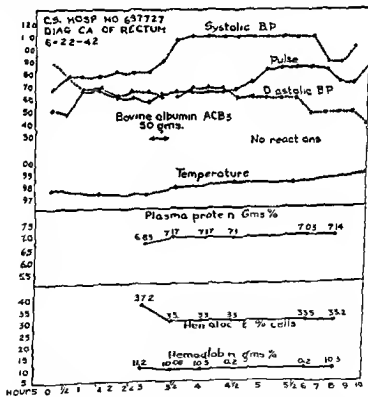


FIG 2—Efficacy of bovine serum albumin in the treatment of shock

BOVINE SERUM ALBUMIN SOLUTIONS IN THE TREATMENT OF SHOCK

CASE 1 (U H No 637727)—G B a white man was 61 years of age. Diagnosis of carcinoma of the rectum with extensive metastases was made. On June 2, 1942, he had bilateral cervical chordotomy for intractable pain secondary to metastases to the lumbar

spine and pelvis. The operation lasted from 3 30 to 5 30 P.M. Although the blood loss was not measured, it was thought not to be excessive. The blood pressure at the start of the operation was 153/74 mm Hg and the pulse 76 per minute. Toward the end of the operation the blood pressure fell to 90/60 mm Hg and the pulse was 82 per minute. During the operative procedure he received 1,000 cc of normal saline solution intravenously. For the first four hours after surgery the blood pressure ranged between 78/52 and 84/60 mm Hg and the pulse between 72 and 90 per minute. During this period he received 1,000 cc of 5 per cent glucose in normal saline solution intravenously and 1,000 cc of 5 per cent glucose in distilled water subcutaneously without appreciable effect on blood pressure or pulse rate. At 9 35 P.M. (approximately four hours after completion of the operation) he was given 50 Gm of bovine serum albumin solution ACB₂ diluted to 200 cc with normal saline solution in twenty minutes. The blood pressure began to rise almost immediately. At 10 P.M., it was 110/64 mm Hg and it remained at about this level until 3 A.M., when observations were discontinued. Although there was little change in the pulse rate, there was a definite improvement in its quality. The hemoglobin (Sahli), hematocrit (Wintrobe tube 3,000 revolutions per minute for thirty minutes), and plasma proteins were taken immediately before the administration of the bovine serum albumin solution and at one half and hourly intervals thereafter. Definite evidence of rather marked hemodilution was noted following the use of the bovine serum albumin solution (Fig. 2).

CASE 2 (U. I. No. 673124)—R. T., a white man, was 43 years of age. Diagnosis of chronic osteomyelitis of the left tibia was made. On March 3, 1942 he had a skin flap applied over a cutaneous sinus, secondary to chronic osteomyelitis of the left tibia. There was considerable bleeding (amount, however, was not measured) and the operation lasted three hours and fifteen minutes. During the first hour of operation, the blood pressure was consistently 170/90 mm Hg and the pulse 96 per minute. During the second hour of operation, the blood pressure fell to 140/70 mm Hg and the pulse rose to 110 per minute. He was then given 500 cc whole blood with no change in blood pressure or pulse. In addition to the blood the patient received 500 cc normal saline solution intravenously during the operation. On returning to his bed in the surgical ward, the patient's blood pressure fell to 60/14 mm Hg and the pulse rose to 118 per minute. He was placed in steep Trendelenburg position but no parenteral fluids were given. During the next forty minutes the blood pressure rose gradually to 80/50 mm Hg but the pulse remained between 100 and 110 per minute. He was then given 100 cc of bovine serum albumin solution CB₂ (25 Gm) undiluted over a period of fifteen minutes. Five minutes after the albumin solution had run in, the blood pressure rose to 100/60 mm Hg and the pulse slowed to 90 per minute. The blood pressure then was maintained adequately between 100/60 to 140/60 mm. Hg until the patient regained full consciousness in two and one half hours. In this same interval the patient also received 500 cc of 5 per cent glucose in normal saline solution intravenously. Unfortunately hemoglobin, hematocrit, and plasma protein values were not obtained.

CASE 3 (U. I. No. 723323)—M. K., a white woman, was 23 years of age. Diagnosis of compound fracture of the right tibia and lacerated tendons of the right leg was made. This patient was injured on Aug. 17, 1941, approximately two hours before coming into the hospital. On admission, she was in acute pain and the skin was cool, moist, and pale. A tourniquet had been in place around the right leg for approximately one hour. The blood pressure, pulse and respiration were respectively 132/70 mm Hg, 90, and 24 per minute. Prior to surgery she was given 100 cc (25 Gm) of bovine serum albumin solution ACB₂ diluted to 200 cc with normal saline solution and during the operation for reduction of the fracture and repair of the tendons she was given an additional 25 Gm. In addition, she received 500 cc normal saline solution during surgery. The operation lasted two hours and fifteen minutes and apart from a temporary fall of blood pressure subsequent to the release of the tourniquet the blood pressure was uniformly maintained between 120/70 and 130/70 throughout and following the surgical procedure. The accompanying chart (Fig. 3) also shows the fall in hemoglobin and hematocrit values indicating definite hemodilution.

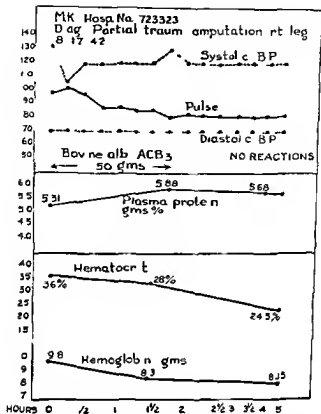


Fig. 3—Efficacy of bovine serum albumin in the treatment of shock

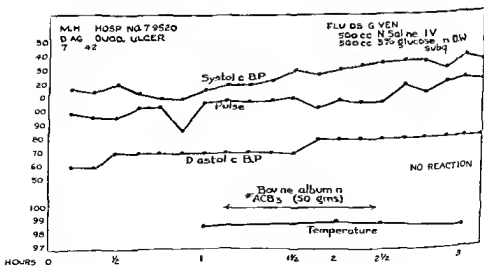


Fig. 4—Efficacy of bovine serum albumin in the prevention of the onset of shock

BOVINE SERUM ALBUMIN SOLUTION IN THE PREVENTION OF THE ONSET OF SURGICAL SHOCK

CASE 1 (U H No 719520)—M H, a white man, was 44 years of age. Diagnosis of duodenal ulcer was made. On July 3, 1942, a partial gastrectomy for duodenal ulcer was done. The duration of the operation was three hours and forty minutes. Blood pressure, pulse, and respiration before the operation were, respectively, 118/60 mm Hg, 100, and 20. At the completion of the surgical procedure they were, respectively, 136/80 mm Hg, 100, and 21, and as can be seen from the chart they were well and uniformly maintained throughout the operation (Fig 4). The blood loss during operation (as determined by measuring the increment in gain of dry sponges²²) was 528 Gm. In addition to 50 Gm of bovine serum albumin ACB, the patient received 500 cc of normal saline solution intravenously and 500 cc of 5 per cent glucose in distilled water subcutaneously.

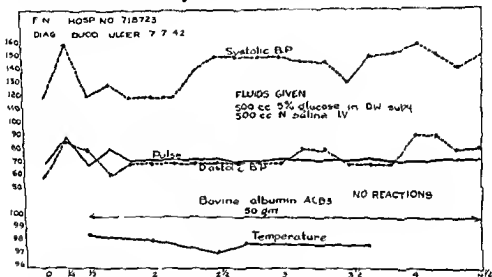


Fig 5—Efficacy of bovine serum albumin in the prevention of the onset of shock

CASE 2 (U H No 718723)—F N, a white man, was 62 years of age. Diagnosis of duodenal ulcer was made. A partial gastrectomy for duodenal ulcer was done on July 7, 1942. The duration of the operation was three hours and forty five minutes. The blood pressure and pulse prior to surgery were respectively, 120/60 mm Hg and 70 per minute. Throughout operation these were well maintained and at the completion of the operation the blood pressure and pulse were, respectively, 150/80 mm Hg and 74 per minute. He received 50 Gm of bovine serum albumin ACB, diluted with 500 cc of 5 per cent glucose in distilled water and 500 cc of normal saline solution intravenously. The blood loss during surgery was 512 Gm (Fig 5).

Discussion—Surgeons have long known that blood is the best agent with which to combat large blood losses. The surgical experience of World War II has lent greater emphasis to this knowledge. In the main, fluid losses sustained by patients are best replaced in kind and in the amount of the loss with a minimal lag interval. The use of dry sponges by surgeons during operation and ascertainment of their accretion in weight²² serves to keep the surgeon informed throughout the operation concerning the extent of the blood loss. For blood losses of 800 cc or less, the administration of plasma in our experience meets

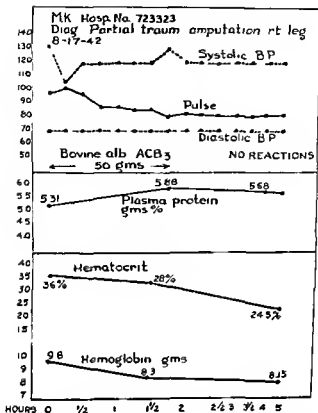


Fig 3—Efficacy of bovine serum albumin in the treatment of shock

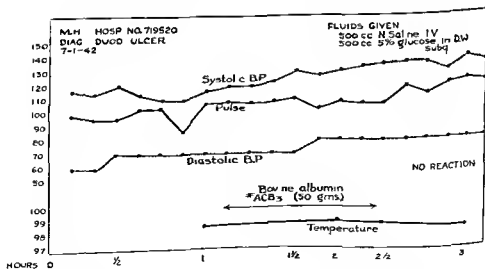


Fig 4—Efficacy of bovine serum albumin in the prevention of the onset of shock

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CASE 1 (U. H. No. 719520)—M. H., a white man, was 44 years of age. Diagnosis of duodenal ulcer was made. On July 1, 1942, a partial gastrectomy for duodenal ulcer was done. The duration of the operation was three hours and forty minutes. Blood pressure, pulse, and respiration before the operation were, respectively, 118/60 mm Hg, 100, and 20. At the completion of the surgical procedure they were, respectively, 136/80 mm Hg, 100, and 22, and as can be seen from the chart they were well and uniformly maintained throughout the operation (Fig. 4). The blood loss during operation (as determined by measuring the increment in gain of dry sponges²²) was 525 Gm. In addition to 50 Gm of bovine serum albumin ACB, the patient received 500 cc of normal saline solution intravenously and 500 cc of 5 per cent glucose in distilled water subcutaneously.

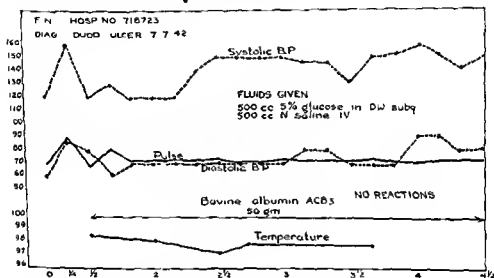


Fig. 5—Efficacy of bovine serum albumin in the prevention of the onset of shock

CASE 2 (U. H. No. 718723)—F. N. a white man was 62 years of age. Diagnosis of duodenal ulcer was made. A partial gastrectomy for duodenal ulcer was done on July 7, 1942. The duration of the operation was three hours and forty five minutes. The blood pressure and pulse prior to surgery were respectively, 120/60 mm Hg and 70 per minute. Throughout operation these were well maintained and at the completion of the operation the blood pressure and pulse were, respectively, 150/80 mm Hg and 74 per minute. He received 50 Gm of bovine serum albumin ACB, diluted with 500 cc of 5 per cent glucose in distilled water and 500 cc of normal saline solution intravenously. The blood loss during surgery was 512 Gm (Fig. 6).

Discussion—Surgeons have long known that blood is the best agent with which to combat large blood losses. The surgical experience of World War II has lent greater emphasis to this knowledge. In the main, fluid losses sustained by patients are best replaced in kind and in the amount of the loss with a minimal lag interval. The use of dry sponges by surgeons during operation and ascertainment of their accretion in weight²² serves to keep the surgeon informed throughout the operation concerning the extent of the blood loss. For blood losses of 800 cc or less the administration of plasma in our experience meets

the demands of the situation satisfactorily. The all too limited experience with bovine serum albumin in the management of shock detailed in the cases cited suggests moreover that with development of a nonantigenic bovine albumin this agent may prove useful in the management of the less serious forms of hematogenic shock.

Of the three cases of shock available for study, two were immediately post operative and the other followed an extensive injury. In the former two cases, the operative trauma and inadequate blood loss replacement were probably primarily responsible for the development of shock. In the last case although the blood pressure was not low the other clinical manifestations of shock were present and in addition a tourniquet which had been applied for one hour had to be removed in order to repair the injured extremity. As Bayliss and Cannon²² showed removal of a tourniquet from an injured extremity might result in shock. Mindful of this bovine serum albumin was given to combat the minor degree of shock on admission as well as preventing an increase in the severity of shock that might have arisen following the removal of the tourniquet or during the ensuing operative procedure. As can be seen from Fig. 3 apart from a very temporary fall in blood pressure after the release of the tourniquet the patient's blood pressure and pulse were well maintained during the operation.

On physiologic grounds albumin whether of human or bovine origin should be an effective agent in drawing fluid from the extracellular tissue spaces into the blood stream. Stead and Ebert²⁷ and Neil Gibson and Jane Way²⁸ have shown that concentrated bovine serum albumin solutions (20 per cent) injected into normal subjects after removal of 10 to 20 per cent of the blood volume by venesection is capable of restoring the blood volume by drawing fluid into the blood stream. The latter group of investigators also showed that there was no essential difference between human and crystallized bovine serum albumins in their ability to draw fluid into the circulation. In this study it can be seen in two of the cases of shock in which the hemoglobin, hematocrit and plasma proteins were taken that there was a marked reduction in the values of the former two indicating a pronounced degree of hemodilution. There was an increase of the plasma proteins in spite of the hemodilution due probably to the added bovine serum albumin which was retained in the circulatory system. In experimental studies Dunphy and Gibson²⁴ have shown that bovine serum albumin is effective in combating burn shock in dogs and Fine and co-workers²⁵ have also demonstrated its efficiency in combating tourniquet shock.

Because a marked hemodilution occurs following the use of hyperosmotic bovine serum albumin solutions these are more effective in dehydrated states when supplemented with adequate amounts of isoosmotic saline or glucose solutions.

EFFICACY OF BOVINE SERUM ALBUMIN SOLUTION IN THE TREATMENT OF INCREASED INTRACRANIAL PRESSURE

CASE 1 (U. H. No. 37459).—M. B., a white girl, was 6 years of age. This patient had sustained a severe cerebral injury on Nov. 14, 1943, following a fall on her head. She

was brought to the University Hospital on Nov 15 1943, in a semiconscious state. Trephine holes were made in the temporal and parietal areas bilaterally to rule out a subdural hematoma but none was found. Her condition grew worse in spite of attempts to reduce intracranial pressure by means of a concentrated sucrose solution intravenously. On Nov 16 1943 she was moribund and as a last attempt to reduce the intracranial pressure, 50 cc (125 Gm) of undiluted bovine serum albumin preparation ACB₁₁ was given intravenously. Approximately one hour later, a definite improvement in the child's condition was noted. She responded to the spoken voice, smiled, coughed and expectorated. On Nov 17, 1943, she was given an additional 8 Gm of ACB₁₁ in 20 cc of saline solution with continued improvement so that it was felt that she would make a complete recovery. On Nov 24 1943, however she died quite suddenly and a post mortem examination revealed the presence of a large occipital subdural hematoma.

Discussion—Since bovine serum albumin molecules do not readily leave the circulatory system they exert a prolonged osmotic pressure which would cause tissue fluid to pass from the extracellular spaces into the blood stream, thus relieving tissue edema. In contrast to this a hypertonic solution of either glucose or sucrose would initially draw fluid from the extracellular spaces into the blood stream. But the molecules would soon leave the circulatory system and pass into the extracellular tissue spaces exerting their osmotic force here, thus tending to draw fluid back from the blood stream into the tissue spaces. Clinically this is paralleled by a temporary reduction in tissue edema followed by a secondary increase which might be greater than the amount present prior to injection.

In all severe head injuries there is some degree of cerebral edema. prolonged reduction of such edema is not possible by means of hypertonic glucose or sucrose solutions for after the initial decrease in intracerebral pressure there is a marked secondary rise. However by means of hyperosmotic bovine serum albumin solutions a more marked and prolonged influence on intracerebral pressure is to be expected on physiologic grounds.

In confirmation of this is the marked clinical improvement of the patient just described. Hypertonic sucrose solution had been used with only slight and temporary improvement and the bovine serum albumin solution was used only as a terminal gesture for it was felt that the patient could not recover.

Unfortunately the subdural hematoma was at a very unusual spot for if trephining and discovery of it could have been done after the improvement of the patient occurred it is not unreasonable to assume that the patient might have made a recovery.

SUMMARY AND CONCLUSIONS

Using highly purified bovine serum albumin fractions obtained by precipitation of bovine plasma by ethanol alcohol at 5° C 469 injections have been made into 410 patients with twelve (29 per cent) immediate reactions and thirty eight (9.2 per cent) delayed reactions. Using bovine plasma and serum, Kremen and associates⁵ noticed an incidence of approximately 50 per cent immediate reactions and 60 per cent delayed reactions. There has thus been a marked reduction in the incidence of immediate and delayed reactions attending the use of purified bovine serum albumin fractions.

the demands of the situation satisfactorily. The all too limited experience with bovine serum albumin in the management of shock detailed in the cases cited suggests moreover that, with development of a nonantigenic bovine albumin this agent may prove useful in the management of the less serious forms of hematogenic shock.

Of the three cases of shock available for study, two were immediately post-operative and the other followed an extensive injury. In the former two cases, the operative trauma and inadequate blood loss replacement were probably primarily responsible for the development of shock. In the last case although the blood pressure was not low, the other clinical manifestations of shock were present and in addition, a tourniquet which had been applied for one hour had to be removed in order to repair the injured extremity. As Bayliss and Cannon²³ showed removal of a tourniquet from an injured extremity might result in shock. Mindful of this bovine serum albumin was given to combat the minor degree of shock on admission as well as preventing an increase in the severity of shock that might have arisen following the removal of the tourniquet or during the ensuing operative procedure. As can be seen from Fig. 3 apart from a very temporary fall in blood pressure after the release of the tourniquet, the patient's blood pressure and pulse were well maintained during the operation.

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EFFICACY OF BOVINE SERUM ALBUMIN SOLUTION IN THE TREATMENT OF INCREASED INTRACRANIAL PRESSURE

CASE 1 (U. H. No. 737452).—M. B., a white girl was 6 years of age. This patient had sustained a severe cerebral injury on Nov. 14, 1943, following a fall on her head. She

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Immediate reactions were of two types (1) anaphylactoid, characterized by dyspnea, cyanosis, and fall in blood pressure (2) pyrogenic, characterized by chills and fever. In the main, the reactions were moderately severe.

The onset of the delayed reactions was usually from twelve to twenty-four days after injection and was characterized by urticaria, erythema, myalgia, arthralgia, and fever. In the severe cases, there were petechiae and ecchymoses.

The incidence of both immediate and delayed reactions was no greater in patients who received multiple injections than in those receiving a single injection.

Skin testing is not an effective means of determining the sensitivity of patients to bovine serum albumin.

Despeciating both purified and crystallized bovine serum albumin with a modification of the method of Edwards¹⁶ has not eliminated immediate or delayed reactions.

Procaine given intravenously (1 Gm. in 200 c.c. saline solution over an interval of one hour) is a very effective agent in the treatment of delayed serum sickness.

No evidences of periarthritis nodosa or pancreatitis were noted in the post mortem findings of seven patients who had received bovine serum albumin but who died of other causes.

In concentrated solutions (25 per cent) bovine serum albumin would appear to be an effective agent in the prevention and treatment of shock. For large blood loss, in excess of 800 c.c., blood obviously would be a more satisfactory agent with which to combat shock.

In dehydrated states isotonic saline and glucose solutions should be given along with the hyperosmotic bovine serum albumin solutions.

In the one instance available for study hyperosmotic bovine serum albumin solution (25 Gm. per cent) was apparently effective in combating cerebral edema.

Because of the persistence of and incapacity caused by the delayed reactions crystallized bovine serum albumin is not recommended at present as an ideal blood substitute. New methods of despeciation may eliminate the antigenicity of bovine serum albumin.

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injection of the concentrated albumin solution. From these determinations, the following data were calculated: (1) Total circulating protein, (2) total circulating albumin, (3) plasma volume increase per gram of albumin injected, and (4) plasma volume increase per gram of albumin retained.

Plasma volume was measured before and at suitable intervals after injection of the albumin by the dye dilution method with T-1624. Determination of total plasma volume was made from one arterial blood sample obtained ten minutes after the intravenous injection of the blue dye. In cases of severe shock, three additional blood samples were withdrawn at successive ten minute intervals to insure a more exact measurement of the plasma volume.⁶ Hematocrits were determined by the method of Wintrobe. In calculating plasma volume changes, account was taken of the blood removed for sampling between successive plasma volume measurements. Serum protein concentrations (Howe method) were determined on blood samples obtained at the time of each plasma volume measurement. The total circulating protein and the total circulating albumin were calculated as the product of plasma volume times the serum protein and the serum albumin concentrations respectively. Protein loss due to sampling between determinations was calculated according to a method described elsewhere.⁷ The plasma volume change per gram of albumin injected was then calculated from the total plasma volume increase in cubic centimeters divided by the total amount of albumin injected in grams. Similarly the plasma volume change per gram of albumin retained was computed from the total plasma volume increase in cubic centimeters divided by the increase in total circulating albumin in grams.

RESULTS

The Effect of the Intravenous Injection of Concentrated Human Serum Albumin Upon Plasma Volume, Hematocrit, and Serum Proteins When Given Without Additional Crystalline Solution—Table I shows the data derived from the study of twenty patients each of whom received concentrated human albumin intravenously without additional intravenous fluids. In Column 1, the patient's initials are given together with the clinical diagnosis. In Column 2, note is made of the time elapsing between the end of the albumin injection and subsequent measurements. The letters "N" and "D" listed in Column 3 denote the fluid state of the patient (whether normal or dehydrated) at the time of the initial study as judged by the history and general clinical appearance of the patient. Column 4 indicates the type of albumin preparation used, and the amount injected in grams.

The values for mean arterial blood pressure, total plasma volume, and hematocrit are given in Columns 6, 7, and 8 respectively. In the next four columns (9, 10, 11, and 12), the serum protein values in grams per cent and the total circulating protein in grams are given.

The distribution of the twenty patients listed in Table I is as follows:

15 postoperative cases (lung and chest wall resections—abdominal surgery)

1 case of marked dehydration due to pyloric obstruction

CHANGES IN PLASMA VOLUME AND MEAN ARTERIAL PRESSURE AFTER THE INTRAVENOUS INJECTION OF CONCENTRATED HUMAN SERUM ALBUMIN IN THIRTY EIGHT PATIENTS WITH OLIGEMIA AND HYPOTENSION

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WITHIN the past three years clinical studies on the intravenous use of concentrated human serum albumin for the treatment of shock and shock like conditions have been undertaken by several groups of investigators¹⁻⁴ The purpose of these studies was to determine the efficacy of this agent in assisting recovery from shock The present report is concerned primarily with a comparison of the effects upon mean arterial blood pressure and plasma volume of the intravenous injection of concentrated human albumin solutions when given with and without additional intravenous fluids In a number of instances the effects of a new salt poor albumin preparation have been compared with those obtained with the standard albumin solution containing 0.3 M NaCl

The results of this study are presented as follows First the data are given on 20 patients each of whom received varying amounts of concentrated human albumin without additional intravenous fluids Of these 7 received the salt poor preparation 13 the standard product Second the data on 18 patients are given each of whom received varying amounts of concentrated human albumin with additional intravenous fluids usually in the form of normal saline solution Six patients in this group were given the salt poor albumin 12 the standard solution

MATERIAL AND METHODS

Various clinical conditions were studied namely postoperative states (extensive resections of the chest wall resections of the lung and various types of abdominal surgery) injuries burns and acute abdominal conditions These included patients with and without shock

Two different solutions of concentrated (25 per cent) human serum albumin were administered the standard albumin solution containing 0.3 M NaCl and the newer salt poor albumin preparation containing 0.04 M Na mandelate or 0.04 M Na acetyl tryptophane

The techniques employed in this study are described in the previous article⁵ In each patient plasma volume hematocrit serum protein concentration and mean arterial blood pressure were measured before and at suitable intervals after

¹ - - - was done under contracts recommended by the Committee
of the Research and Development and Columbia
The Commonwealth Fund

injection of the concentrated albumin solution. From these determinations, the following data were calculated: (1) Total circulating protein, (2) total circulating albumin, (3) plasma volume increase per gram of albumin injected, and (4) plasma volume increase per gram of albumin retained.

Plasma volume was measured before and at suitable intervals after injection of the albumin by the dye dilution method with T 1824. Determination of total plasma volume was made from one arterial blood sample obtained ten minutes after the intravenous injection of the blue dye. In cases of severe shock, three additional blood samples were withdrawn at successive ten minute intervals to insure a more exact measurement of the plasma volume.⁶ Hematocrits were determined by the method of Wintrobe. In calculating plasma volume changes, account was taken of the blood removed for sampling between successive plasma volume measurements. Serum protein concentrations (Howe method) were determined on blood samples obtained at the time of each plasma volume measurement. The total circulating protein and the total circulating albumin were calculated as the product of plasma volume times the serum protein and the serum albumin concentrations, respectively. Protein loss due to sampling between determinations was calculated according to a method described elsewhere.⁷ The plasma volume change per gram of albumin injected was then calculated from the total plasma volume increase in cubic centimeters divided by the total amount of albumin injected in grams. Similarly the plasma volume change per gram of albumin retained was computed from the total plasma volume increase in cubic centimeters divided by the increase in total circulating albumin in grams.

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- 1 case of marked dehydration due to pyloric obstruction

TABLE I PLASMA VOLUME AND PLASMA PROTEIN CHANGES FOLLOWING INJECTION OF CONCENTRATED HUMAN ALBUMIN

PATIENT AND DIAGNOSIS	TIME	FLUID STATUS	ALBUMIN INJECTED (GM)	FLUID WITH ALBUMIN (G.O.)	MPV ART BT (MM)	PLASMA VOL (CC)	HEMA TOCIT (%)	ALBU MIN (%)	PLASMA GLOBU- LIN (%)	TOTAL G.O. (GM)	PLASMA VOLUME CHANGE PER GM. ALBUMIN INJECTED
1 Y C. PO paratyphoid	7 m p	N	24 (9 P)	-	55	2410	40	24	25	59 142	-
2 K C. PO thoracoplasty	16 m p	-	48 (8 P)	-	42	2955	78	15	26	61 150	26
3 Y P PO thoracoplasty	15 m p	-	40	-	50	2210	72	50	24	74 166	5
4 J O. PO leukemia	21 m p	-	40	-	74	1855	79	12	19	60 123	-
5 L. L. PO thoracoplasty	15 m p	-	40	-	56	2900	68	14	22	70 203	21
6 H E. acute pancreatitis	10 m p	-	40	-	12	2240	41	45	21	60 148	-
7 S J PO leukemia	12 m p	-	48	-	54	2532	25	13	24	61 155	21
8 A L. PO strangulated hernia	18 m p	-	48	-	42	3695	29	44	21	65 209	28
9 C B. Traumatic lacerations alcoholism	5 m p	-	48	-	61	2200	41	24	20	40 112	-
10 S H. PO gastric ulcer	11 m p	-	48	-	12	2973	76	41	17	58 172	17
					10	2475	75	38	17	55 163	16
					60	2420	76	41	24	71 172	-
					45	2910	73	40	24	77 212	10
					48	2550	43	26	17	43 109	-
					42	3705	76	41	11	71 178	10
					48	2902	78	41	12	73 151	5
					41	2210	42	17	20	58 177	-
					52	3100	78	42	20	62 210	8
					24	1600	79	34	21	65 89	-
					117	1875	71	34	14	68 125	8
					123	2150	29	48	11	62 144	15

11	K C I O thoracoplasty	21 m l 3 h l	-	50 (S P)	-	59	2440	35	24	22	67	164	-	11
						70	3230	25	48	22	71	209	16	12
						77	3120	25	46	21	67	209	14	
12	X C I O thoracoplasty	17 m l 3 h p	-	50 (S P)	-	64	2410	38	22	37	62	150	-	11
						80	3090	36	40	28	68	210	16	9
						91	2386	35	41	26	67	173	6	
13	J R Exposure to col	14 m l	N	50 (S P)	-	59	2810	35	25	34	74	210	-	14
						47	3290	33	41	37	78	257	12	
14	Q P I O thoracoplasty	-0 m p 4 h p	N	45	-	18	2236	37	40	18	58	130	-	20
						70	2730	29	42	18	60	166	11	11
						70	3050	29	46	19	64	192	17	
15	R S P O thoracoplasty	17 m p 2 h 37 m p	N	50	-	93	2241	38	34	28	62	139	-	9
						103	2540	35	43	26	60	176	12	14
						99	2712	35	41	26	67	180	19	
16	G F P O lobectomy	31 m p 3 h 32 m p	N	50	-	52	2972	18	42	21	63	188	-	12
						88	3240	13	15	28	63	204	3	0
						94	3622	35	46	16	62	228	13	
17	L V Mesenteric thrombosis	21 m p 2 h 13 m l	D	47	-	66	1366	55	26	32	58	80	-	6
						86	1630	50	54	13	67	109	6	11
						94	1910	47	45	14	59	113	12	
18	I I Pyloric obstruction	1 h p	D	0	-	68	2739	30	31	19	50	137	-	20
						75	3168	27	41	13	54	171	0	
19	H G P O thoracoplasty	17 m p 1 h 20 m p	N	47	-	75	2241	32	32	17	40	110	-	0
						75	2349	26	42	21	64	163	7	10
						76	2712	24	44	32	66	179	10	
20	A B P O pneumectomy	46 m l 2 h 25 m p	N	50	-	62	1870	48	45	09	53	99	-	9
						82	2100	38	53	18	71	140	5	10
						87	2090	34	51	17	68	141	4	

* Normal D dehydrated
 † S P Salt poor albumin all other patients received albumin solution containing 0.3 M NaCl

- 1 case of irreversible peripheral circulatory failure due to exposure to cold
- 1 case of extensive lacerations in a patient with acute alcoholism
- 2 cases of acute abdominal conditions (incarcerated hernia and thrombosis of mesenteric artery)

Of these 20 patients treated with concentrated human albumin solution only 17 recovered without the aid of additional intravenous therapy. One patient (Case 2) because of continuous bleeding received a blood transfusion four hours after the second period of observation. The 2 remaining patients (Cases 6 and 13) who were critically ill on entry to the hospital died shortly after completion of the third study. It is of interest that although Patient 9 was in mild shock, Patient 17 in moderately severe shock, and Patient 18 in a state of severe dehydration at the time of the first study, all 3 recovered without the aid of additional fluid therapy.

In the majority of instances measurements were repeated within twenty five minutes of completion of the albumin injection. In four instances however *this was made between thirty and sixty minutes after completion of the injection.* Eleven patients in this group were studied a third time approximately 2½ hours after the injection had been completed.

One-half hour after the end of the albumin injection the average rise in mean arterial pressure for all 20 cases was 15 mm Hg. It may be seen in Table I however that in two instances there was no rise in blood pressure (Cases 6 and 19) and in one instance there was a fall of 12 mm Hg (Case 13). If the 2 patients (Cases 6 and 13) who failed to survive are excluded from the calculation the average rise in mean arterial blood pressure for this group was 17 mm Hg.

The intravenous injection of concentrated albumin was associated in every case with an increase in plasma volume and a fall in hematocrit. The average increase in total plasma volume for all 20 cases one-half hour after an average albumin injection of 46 Gm was 520 c.c. Individual increases ranged from 104 to 1363 c.c. The average increase in plasma volume per gram of albumin injected for the group was 12 c.c. With respect to those individual patients (Cases 2, 9, 10, 17, 19, and 20) in whom there was continuous blood or plasma loss the plasma volume increase per gram of albumin injected and per gram of albumin retained was expectedly smaller, the average being 7 c.c.

Determinations made upon 11 patients 2½ hours after the injection showed no consistent change in total plasma volume. There was an average further increase of 297 c.c. in 6 cases, an average loss of 207 c.c. in 4 cases, and no change in 1 case. However figures for the average rise in mean arterial blood pressure and the average increase in plasma volume per gram of albumin injected and retained did not differ significantly from those found at the time of the second period.

Four postoperative thoracoplasty patients receiving the salt poor albumin solution and 5 comparable patients receiving the standard albumin solution were selected for comparison of the two preparations. Figures for the average

change in each of the measurements made one half hour after the albumin injection are given in Table II

It may be seen in Table II that the effects of the salt poor albumin were, on the whole, similar to those of the salt-containing solution

TABLE II COMPARATIVE EFFECTS OF TWO PREPARATIONS OF CONCENTRATED HUMAN ALBUMIN

	INCREASE IN MEAN PRESSURE (MM HG)	FALL IN HEMATOCRIT (%)	PLASMA VOLUME INCREASE C C PER GRAM ALBUMIN INJECTED	RETAINED
Average for 4 patients receiving salt poor solution	16	5	15	14
Average for 4 patients receiving standard solution	10	7	16	16

The Effect of the Intravenous Injection of Concentrated Human Serum Albumin Upon Plasma Volume, Hematocrit and Serum Proteins When Given With Additional Crystalline Solution—The data in Table III have been derived from the study of 18 patients who received at least 400 cc of additional crystalline solution, with 2 exceptions (Cases 2 and 17), in the form of normal saline solution, along with each unit of concentrated albumin, the unit consisting of 25 Gm of albumin in 100 cc of fluid

The distribution of the 18 cases reported in Table III are as follows

- 10 postoperative cases (lung and chest wall resections—
abdominal surgery)
- 4 cases of burn
- 2 cases of acute abdominal conditions
- 1 case of multiple lacerations
- 1 case of gunshot wounds of the abdomen

With the exception of the cases of burn and peritonitis where plasma loss was continuous over a considerable period of time, no additional intravenous therapy was administered. The immediate response to treatment was favorable in all cases.

Measurements were made in this group for the second time approximately one hour after the completion of therapy rather than at twenty five minutes as in the first group. In twelve instances a third set of measurements was made three hours after therapy had been completed.

The average rise in mean arterial blood pressure in this group at the time of the second period was comparable to that observed in the group receiving concentrated albumin solution alone (17 mm Hg). However, in 3 patients (2 cases of burn and 1 case of postoperative thoracoplasty) there was little or no change in blood pressure after the administration of the albumin together with about 1,000 cc of normal saline solution.

The increase in plasma volume and the fall in hematocrit following treatment in this group of patients was similar to, although larger than, that seen

TABLE III PLASMA VOLUME AND PLASMA PROTEIN CHANGES FOLLOWING INJECTION OF CONCENTRATED HUMAN ALBUMIN

PATIENT AND DIAGNOSIS	TIME	FLUID STATE*	ALBUMIN INJECTED (GM)†	FLUID WITH ALBUMIN (CC)	MEAN APT BE (MM)	PLASMA VOL. (CC)	HEMA TOCRIT %	PLASMA PROTEIN		PLASMA VOLUME CHANGE PER GM ALBUMIN INJECTED	ALBUMIN RETAINED
								ALB. MIN %	GLOB. MAX %		
1 K S infant edema	13 m	N	50	800	77	800	42	19	23	62	174
					100	3430	74	44	16	60	206
2 M S 2 yr 10% burn	3 h, 43 m	N	100	800	91	2800	48	40	17	55	154
					34	3375	44	45	33	56	169
3 M H, P O thoracoplasty	50 m	N	50	1000	42	2392	28	36	21	54	129
	1 1/2 h				73	3231	22	41	17	60	104
					16	2967	21	40	15	55	158
4 B D, P O thoracoplasty	43 m	N	48	500	38	1905	23	38	22	60	114
	3 h, 8 m				91	710	22	42	13	55	208
					97	700	21	40	14	54	105
5 V W P O thoracoplasty	49 m	N	50 (S P)	1000	19	60	40	42	17	70	180
	3 h, 10 m				70	2680	29	47	10	57	153
					75	3070	25	46	10	56	172
6 M R gunshot wound P O	1 h, 40 m	N	52 (S P)	1000	50	2000	50	43	14	77	128
	2 h, 51 m				78	3270	42	44	10	54	175
					72	2375	44	45	11	56	131
7 W S ext lacerations	1 h 10 m	N	44 (S P)	1000	40	1740	38	43	15	58	101
					55	2470	29	48	12	60	148
8 B D P O thoracoplasty	29 m	N	50 (S P)	1000	61	2600	37	42	10	62	161
	3 h 28 m				70	3150	20	46	15	61	192
					54	3710	9	46	15	63	226

No.	O, W, P, O thoracoplasty	N	A 55 m 3 h, 9 m	P 50	P 800	G	1750	38	42	20	62	108	17	19
10	M O, P O thoracoplasty	N	41 m 3 h, 45 m	50 (S P)	800	80	2570	24	47	13	57	146	12	16
11	A O, P O lobectomy	N	20 m 2 h, 56 m	50	800	66	2520	41	43	21	64	161	13	15
12	M S, P O pneumectomy	N	25 m 2 h	50	800	67	2590	35	37	28	61	158	31	21
13	M M, 21 hr F 50% turn	D	18 m 2 h	50	1200	93	2960	40	43	21	63	180	8	12
14	K P, 5 hr F 50% turn	D	28 m 2 h	50	1000	80	2760	60	27	34	61	00	7	13
15	A D, 3 hr F 25% turn	D	1 h, 32 m	25	900	84	2370	45	40	29	09	104	0	12
16	I S, P O thoracoplasty	N	15 m 3 h	40	1000	82	3732	34	40	23	70	202	18	23
17	S P, P O, rup tured vascu	D	1 h 2 h, 42 m	74.5	800	74	3130	41	28	21	49	154	4	27
18	W H, incar cerated hernia	D	41 m 2 h	25 (S P)	1200	51	3100	41	26	22	58	180	22	21

*N, Normal D, dehydrated
 15 P, Salt poor albumin all other patients received albumin solution containing 0.3 M NaCl

in the previous group. The average increase in total plasma volume for all 15 patients one hour after an average albumin injection of 52 Gm was 711 cc. The average increase in plasma volume per gram of albumin injected was 15 cc. Calculated on the basis of each gram of albumin retained, the increase in plasma volume amounted to 16 cc. As in the first group, the plasma volume increase per gram of albumin injected and per gram of albumin retained was significantly lower (8 cc) in the patients with burn and peritonitis in whom there was continuous loss of plasma.

In the 12 patients in whom a third set of observations was made, changes, although inconstant, indicated a trend toward loss of plasma volume rather than gain when compared to the results obtained in the 11 patients of the preceding group who received albumin alone. Nine cases showed a loss of plasma volume averaging 292 cc whereas only 3 showed an increase averaging 520 cc. Measurements of mean arterial blood pressure and of plasma volume per gram of albumin injected and retained gave approximately the same values at three hours as those obtained within the first sixty minutes after completion of the combined albumin saline therapy.

The effects of the salt poor albumin solution given with additional saline to 6 patients in this group did not appear to differ significantly from those seen in the 12 patients receiving the standard preparation together with saline solution.

DISCUSSION

The intravenous administration of concentrated albumin solution given with or without additional fluid in two groups of 20 and 18 patients, respectively, was free from untoward clinical reactions. In most instances, the albumin solution was given rapidly, usually over a period of fifteen minutes or less.

In general, the injection of concentrated human albumin solution alone was associated with an immediate increase in plasma volume of approximately 12 cc per gram of albumin injected. Essentially the same average figure was found for each gram of albumin retained. According to the studies of Seatchard

18 cc per
patients
its theo-

retical osmotic activity

The intravenous administration of 400 cc of isotonic saline solution along with the albumin solution resulted in a somewhat greater increase in plasma volume per gram of albumin both injected and retained, the average being 16 cc. This figure compares more favorably with the theoretical value of 18 cc. With respect to the osmotic activity of concentrated albumin *in vivo*, the volume of fluid held by each gram of albumin in the experience of others covered a considerable range. In the series of Courmand and associates,² each gram of albumin retained held 17 cc of fluid. In the series of Warren and associates,³ the figure was 10 cc. In the series of Stead and co-workers,⁴ the figure was 14 cc. This range of values is, perhaps, to be expected on the basis of (1) differences in the degree of hydra-

tion of patients (2) differences in the amount of fluid given intravenously along with the albumin and (3) differences in the type of clinical condition (medical traumatic etc.) studied

Patients in severe shock presumably with continuing blood or plasma loss, showed much smaller increases in plasma volume per gram of albumin given and retained (8 cc average in shock against 14 cc average in nonshock cases). In a case of severe shock therefore the administration of 100 cc of concentrated albumin (20 per cent) without additional fluid corresponds to no more than 200 cc of plasma.

Although in the majority of instances the increase in total circulating protein after the injection of albumin was approximately equal to the amount given it should be noted that in 25 per cent of the cases studied this increase was significantly greater than expected. This observation suggests the possibility that during recovery protein may be mobilized from body reserves or that blood in static pools during the hypotensive period may be returned to the circulating blood stream as the state of the general circulation improves. Errors in laboratory determinations are of course a possibility but the gain in protein over and above the amount injected far exceeds that considered due to the error of the method that is +0.2 per cent.

In spite of the fact that a rise in intra-arterial blood pressure followed the intravenous injection of concentrated albumin in group I and of concentrated albumin with additional fluid in group II the blood pressure failed to reach accepted normal levels. This observation has been noted previously by Courmand and associates⁷ who studied the effects of concentrated human albumin therapy upon the dynamics of the circulation. Their results showed clearly that changes in mean arterial blood pressure are not a reliable index of changes in cardiac output and that although cardiac output and intra-auricular pressure (venous return) attain normal levels after the intravenous injection of concentrated albumin solution the blood pressure may remain subnormal. It was also pointed out that with hemodilution there would be a decrease in blood viscosity. This may account at least in part for the failure of the blood pressure to rise to accepted normal levels. Further evidence that changes in viscosity play an important role in the variation of peripheral resistance was obtained in a study on the intravenous use of a gelatin solution of high viscosity in the treatment of shock.⁸ In this latter study the increase in blood pressure was relatively greater than the increase in cardiac output.

Of 3 patients in the first group (Cases 6, 13, and 19) who showed no increase in mean arterial blood pressure after the injection of albumin it is of interest to note that the one patient who survived (Case 19) was the only one of the three who did not show a significant increase in plasma volume. In contrast the 2 patients who seemed from the start beyond the resources of replacement therapy and who later died showed a rapid increase in plasma volume. It is suggested that this latter sequence of events may be of some prognostic value. A rapid increase in plasma volume in the presence of a stationary or falling blood pressure after the intravenous injection of albumin may indicate failure in vasomotor tone.

A further point of interest lies in the fact that these 2 patients (Cases 6 and 13) returned as much albumin in the circulation as did the surviving group of patients. This observation speaks against the concept that a generalized increase in capillary permeability is characteristic of irreversible shock.

CONCLUSIONS

1 In a group of 20 patients requiring fluid replacement, the intravenous injection of concentrated human albumin solution given without additional intravenous fluid was associated with a fall in hematocrit and a rapid increase in plasma volume amounting to 12 cc per gram of albumin given. Approximately the same average figure was found per gram of albumin retained. The average increase in plasma volume in the 6 patients who were in shock was smaller than the average for the entire series (7 cc per gram of albumin injected and retained).

2 The administration of 400 cc of isotonic saline solution along with the albumin solution to a group of 18 patients resulted in a greater increase in plasma volume as compared to the increase when albumin solution was given alone. 15 cc per gram of albumin injected. 16 cc per gram of albumin retained. In the cases of burn and peritonitis where there was continuous plasma loss increases in plasma volume after the combined albumin saline therapy were expectedly smaller (8 cc per gram of albumin injected and retained).

3 The average injection of 46 Gm. of concentrated human albumin solution alone produced an average rise in mean arterial blood pressure of 17 mm. Hg. The same average rise was observed after the administration of albumin together with additional intravenous saline solution.

4 The effects of the salt poor albumin solution given with and without additional saline solution did not differ significantly from those of the standard salt containing albumin solution given with and without additional saline solution.

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ACUTE PHLEGMONOUS GASTRITIS

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ACUTE phlegmonous gastritis is a nonspecific infection of the stomach wall characterized by seropurulent or fibrinopurulent inflammation usually involving all the gastric layers to some extent, but affecting chiefly the submucosa.

Although first described by Galen, the condition has been reported relatively infrequently in the literature. The first case described in modern medical writing was reported by Cruveilhier in 1820. By 1905, 50 cases were collected, in 1919 Sundberg¹ reviewed a series of 215 cases including 17 cases of his own. In 1937 Fink² was able to bring the total to 306. Approximately 29 new cases have been described during the past nine years, for a total of 335 cases to date.

The etiology of acute phlegmonous gastritis is not entirely clear, although a number of theories have been advanced.³ The organism involved, when cultures have been taken is hemolytic streptococcus in over 70 per cent of the cases.⁴ Many other organisms have been encountered however, including staphylococcus, pneumonococcus, *Bacillus coli*, *Bacillus subtilis*, *Bacillus proteus*, and *Bacillus welchii*.⁵

The pathologic process may be initiated in one of two ways, either as a local condition or metastatic from a distant focus of infection. In the former, some pre-existing pathologic condition such as carcinoma atrophic gastritis ulceration associated with corrosive poisoning or a surgical procedure on the stomach, allows the initiation of the inflammatory process. It is somewhat difficult to visualize how the infecting organisms are able to remain active in the presence of gastric secretion but as Sundberg pointed out, many of the patients falling into this locally initiated group have a hypoaclidity for one reason or another. In line with this Symmers was able to show that dogs suffered no ill effects when fed a mixture of streptococci and ground glass.⁶ However, Doehle has produced phlegmonous gastritis by feeding streptococci to dogs whose stomach mucosa had previously been damaged by alcohol ingestion.

In the larger group of patients no definite break in the mucosa is found and it is believed that the infection is metastatic possibly on an embolic basis, from a distant focus of infection. Cases have been reported following tonsillitis (Brooks and Clinton),⁷ stomatitis, furunculosis (Gerster),⁸ otitis media (Barnett and Harris),¹⁰ erysipelas drainage of an oral infection, or extraction of an infected tooth. Mortland and Eisenberg¹¹ noted that several cases were found at autopsy associated with a puerperal sepsis epidemic in Prague in 1847, though the condition is rare as an accompaniment of a septicemia.

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A further point of interest lies in the fact that these 2 patients (Cases 6 and 13) retained as much albumin in the circulation as did the surviving group of patients. This observation speaks against the concept that a generalized increase in capillary permeability is characteristic of irreversible shock.

CONCLUSIONS

1 In a group of 20 patients requiring fluid replacement, the intravenous injection of concentrated human albumin solution given without additional intravenous fluid was associated with a fall in hematocrit and a rapid increase in plasma volume amounting to 12 cc per gram of albumin given. Approximately the same average figure was found per gram of albumin retained. The average increase in plasma volume in the 6 patients who were in shock was smaller than the average for the entire series (7 cc per gram of albumin injected and retained).

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4 The effects of the salt poor albumin solution given with and without additional saline solution did not differ significantly from those of the standard salt containing albumin solution given with and without additional saline solution.

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ness is localized to the epigastric area until a spreading peritonitis develops. It was noted by Deminger in 1879 that the pain in phlegmonous gastritis is relieved when the patient sits up (Deminger's sign). Fluoroscopic examination of the upper gastrointestinal tract reveals an atonic stomach with loss of the mucosal pattern, and barium retention may be complete.

Among the various conditions which must be considered in the differential diagnosis of acute phlegmonous gastritis are perforated ulcer (either gastric or duodenal), acute pancreatitis, acute cholecystitis, cholelithiasis, and basal pneumonia. However, only one author has reported making this diagnosis correctly, and it usually becomes apparent only at operation or necropsy.²⁰

The treatment as reported in the literature has not yielded very encouraging results.²⁻²¹ Gastric resection has been performed on some patients but the mortality is practically 100 per cent unless one is dealing with the localized form of the disease which may respond to this treatment. Cutler and others have used a simple gastrotomy with success. Elhason and Murray Wright have suggested a gastrotomy with incision of the mucosa for drainage into the gastrointestinal tract. In the very rare cases in which the patients recover without operation this process may occur spontaneously and thus allow satisfactory drainage without peritonitis or a walled off abscess may form which could result in the chronic type of the disease.¹

In the case we are reporting the operative procedure was similar to that used by Elhason and Murray Wright which employs the sound surgical principle of drainage of an abscess cavity. If no localization is found, it is doubtful that any operative procedure on the stomach is justified. Since the infecting organism in this case was the hemolytic streptococcus as it is in the majority of them penicillin was used in large doses and we feel this was significantly responsible for the patient's relatively benign postoperative course.

CASE REPORT

The patient was an 18 year old white male who had been admitted to the hospital on May 19, 1946 with a diagnosis of measles. He had previously been in good health with no history of gastrointestinal disturbances. On the afternoon of May 31, 1946 after what had been an uneventful convalescence the patient complained of the sudden onset of a rather severe nonradiating epigastric pain accompanied by nausea but no vomiting. Examination revealed acute well localized epigastric tenderness with some spasm but no rigidity. Temperature was 100° F, pulse 90, respirations were 28. White blood cells were 24,000 with 72 per cent polymorphonuclear cells. X-ray view of the chest was negative and a roentgenogram of the abdomen revealed no gas beneath the diaphragm. Bowel sounds were present. He was placed on penicillin and watched through the night.

The following morning the patient's temperature had dropped to 99.2° F, pulse and respirations remained the same. There was no change in the physical examination at this time. Serum amylase level was 114 units. During the course of the day however, the epigastric pain began to increase in severity and to become somewhat less localized. Rebound tenderness referred to the epigastrium was noted. There was still no vomiting. By afternoon the temperature had risen to 101.4° F, pulse 100, respiration 32. The chest was clear to auscultation. Only an occasional bowel sound was present in the lower abdomen. White blood cells remained at 24,000, urine examinations were negative. Surgical intervention was decided upon and a preoperative diagnosis of perforated gastric ulcer was made.

In 80 per cent of the cases the patients fall into an age group of from 30 to 60 years and the condition is three times as common in men as in women.¹⁰ When the disease occurs in younger individuals it is usually associated with an acute infectious process such as measles scarlet fever, or streptococcal pharyngitis as in the case reported by Cutler and Harrison.¹²

Early observers of phlegmonous gastritis described the post mortem findings as a "carbuncle of the stomach" (Virchow) or as erysipelas of the stomach the cutaneous analogy being striking after examination of the pathologic material. Two varieties of the disease are described, the localized and the acute diffuse types. In the former, a classical example of which was reported by Novak,¹⁴ the process is well demarcated and consists of a walled off abscess cavity involving chiefly the submucosa with some destruction of the muscularis the original inflammatory reaction usually has resulted in numerous adhesions to surrounding structures. The early symptoms of this type are somewhat similar to those of the acute form and the chronic phase may be the end result of an acute attack.¹⁵ With the establishment of the abscess cavity, the symptoms are chiefly those of obstruction caused by the tumor mass.

In the acute diffuse form, the entire stomach or merely a portion of it may be involved.¹⁶ It is usually stated that the process shows sharp limitation to the stomach alone, although Greaves reported two cases discovered at autopsy where a part of the duodenum was also involved.¹⁷ The process may vary from early inflammation in some areas to complete gangrene with perforation in others. The mucosa is usually intact and shows evidence of lymphocytic infiltration and edema. There may be thromboses present and also areas where extravasation of blood has taken place. As in the localized form, however the major pathologic changes are found in the submucosa which may form two thirds of the thickness of the gastric wall. In this layer the typical severe inflammatory reaction accompanied by massive polymorphonuclear infiltration is encountered. The muscularis and serosal layers show varying degrees of involvement from edema to necrosis depending on the extent of the primary process in the submucosa. Untreated the process resolves by perforation either into the gastrointestinal tract which may result in a spontaneous cure or into the abdominal cavity causing a peritonitis which is fatal in over 90 per cent of the cases. Death may occur without peritonitis however and it is believed to be the result of the toxemia accompanying the disease.¹⁸ Early recognition or suspicion of the condition however followed by prompt and adequate therapy may alter this grave prognosis in the future.

The signs and symptoms of the disease in its acute form are those of an acute lesion in the upper abdomen plus sepsis.¹⁹ Severe epigastric pain is generally the earliest symptom it is rather sudden in onset continuous and quite well localized before perforation. Vomiting is usually but not necessarily present and contrary to what might be expected the vomitus rarely contains pus. The temperature and pulse rate are usually high and a leucocytosis of 20 000 to 30 000 with a marked shift to the left is common. The pain is localized, not referred to the back and usually becomes continuously worse. Tender

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The abdomen was opened through a high right transrectus incision, and a slightly turbid fluid was encountered free in the peritoneal cavity. The stomach was found to be markedly indurated in the distal two thirds, but the process stopped abruptly at the pylorus. Low in the ntral indurated portion there was a fluctuant mass measuring about 3 cm. in diameter over which the omentum had become adherent. On aspiration this yielded frank pus and blood.

After carefully walling this area off with lap jale the abscess was opened. The mucosa underlying it was found to be intact, and an opening was made into it allowing drainage into the stomach cavity. The incision into the abscess was then closed with four heavy sutures through the serosa and muscularis and the omentum was tacked down over the area. Five grams of sulfanilamide powder were placed in the peritoneal cavity. The wound was closed without drainage. Culture of the material aspirated from the abscess yielded hemolytic streptococci.

The patient was placed on continuous Wangensteen suction postoperatively, he received daily 1000 cc 5 per cent dextrose in distilled water, 1000 cc five per cent dextrose in normal saline solution, and either 1000 cc of amigen or 500 cc of whole blood according to his requirements which were followed by frequent blood counts and blood chemistries. He was also given penicillin (50,000 units every three hours) and intravenous sodium sulfadiazine 2.5 Gm. twice daily. He passed some gas per rectum on the second postoperative day although the stomach did not empty well until the seventh postoperative day when the Levine tube was removed. Temperature had returned to practically normal on the third and fourth postoperative days, but on the fifth postoperative day it started to rise again. White blood cells were 7,500 and urine was negative. The wound was healing well without evidence of infection and examination of the abdomen showed minimal tenderness. The chest was clear and there was no evidence of phlebitis. Although the blood level of sulfadiazine was only 4.4 mg per cent it was felt that the fever was due to reaction to the medication. Sulfadiazine was stopped on the eighth day and while the temperature rose to 103° F that day it rapidly returned to normal on the following day and remained essentially so for the rest of the hospitalization period.

Two weeks postoperatively he was up and around and on a high protein diet. Penicillin was stopped on the eighteenth postoperative day. The patient had lost about twenty pounds during the course of the illness. In spite of eating rather well, however, he failed to gain weight and the plasma proteins remained around 5.5 Gm per 100 cc. He was unable to tolerate a high protein high caloric formula or oral amigen so amigen or plasma were given intravenously for ten days. At the end of this time he had gained five pounds, the proteins rose to 6.40 Gm per 100 cc and he felt much stronger. Four weeks postoperatively he was sent home on a twenty day leave.

On return to the hospital the patient looked well although he had not gained any more weight. Fluoroscopic examination of the stomach at this time revealed a perfectly normal stomach mucosa; there was no demonstrable evidence that an operative procedure had been performed. The patient was discharged to duty three months after operation.

SUMMARY

A discussion of the problem of acute phlegmonous gastritis has been presented. The mortality in previously reported series varies from 64 to 92 per cent.

A case was reported in which the patient was treated with gastrotomy for drainage of a fluctuant area which was part of a diffuse inflammatory process. Adequate doses of penicillin were given postoperatively in combination with intravenous sulfadiazine. The patient recovered.

It is believed that, where the organism involved responds well to antibiotic agents, adequate surgical drainage of localized abscesses in conjunction with use of the indicated drug may well bring about a significant reduction in the present mortality figures for this disease.

among these are foreign bodies, instrumentation, and perforation of a pre-existing lesion such as diverticulum, ulcer, or carcinoma

Smead (quoted by Wagner) reported a case of esophageal perforation below a stricture in a 50 year old man who was known to have a chronic duodenal ulcer. A preoperative diagnosis of perforated duodenal ulcer was made, however, at operation a volvulus of the lower bowel was discovered. The patient died thirty six hours following the operation. Autopsy findings were pyloric stenosis collapse of the left lung pleural empyema, an esophageal stricture 5 cm above the diaphragm and, between this and the diaphragm, a 2 cm long perforation into the mediastinum and left pleural cavity.

Smead explained the perforation on the basis of vomiting as a result of the volvulus. Because of the pyloric stenosis and esophageal stricture, the stomach could not empty quickly enough during the act of vomiting and a perforation resulted.

We have had the opportunity of observing four cases of perforation of the esophagus into the mediastinum and/or pleural cavity. In two of the patients the etiology was peptic ulcer of the lower esophagus and cardioesophageal junction.

In the others the perforations were secondary to instrumentation. Three of the patients died within a short period of time following the initial symptoms. The fourth patient apparently experienced a perforation high in the esophagus with a resultant emphysema of the neck and mediastinitis. The pleura was not involved and she made an uneventful recovery.

The two patients showing ulcers had been consuming alcoholic beverages at or shortly prior to the onset of symptoms. In each a considerable quantity of alcoholic smelling pleural fluid was withdrawn before death in an effort to alleviate the discomfort in the chest. It is interesting that in three cases reported by Eliason and Welty the perforations in two were preceded by bouts of vomiting and retching. One of these was a known alcoholic who had recently been on a prolonged drinking spree. Perforation in the third patient followed an operation for a low small bowel obstruction. While vomiting had preceded the perforation in this case it was not considered by the authors to be a prominent feature in the history. In cases of esophageal perforation observed by Raestrup, Vinson, Girard and Kessel (quoted by Wagner) the seat of the perforation arose by sudden overstraining of the esophagus caused by either severe choking or vomiting.

It would appear from reviewing the literature and also from the following histories in two of our cases that a sudden increase in pressure such as that resulting from a blow to the abdomen or from vomiting and retching, is a contributing factor in the etiology of spontaneous esophageal perforation.

CASE REPORTS

CASE 1—The patient a 51 year old white man was admitted to the Buffalo General Hospital late in the evening with the history of headache, nausea and precordial pain since afternoon. Just before supper he took several drinks of whiskey thinking it would settle his stomach. Before eating suddenly he became extremely nauseated. This was followed by vomiting and sharp precordial pain which radiated to the lower left side of the chest, abdomen and left groin.

THE RADIOGRAPHIC DIAGNOSIS OF PERFORATIONS OF THE UPPER GASTROINTESTINAL TRACT INTO THE MEDIASTINUM AND PLEURAL CAVITY

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DESPITE the advances made in recent years in the diagnosis and treatment of lesions of the esophagus one lesion still presents an extremely high mortality rate, namely, esophageal perforation. As Wagner stated in his very fine paper on the subject, "The tragic fate (esophageal perforation) can almost never be averted by surgical intervention, even if the surgery is carried out by the most skillful surgeon."

Fortunately this is not always the case, as the prognosis depends in part on the location of the perforation in the esophagus. Perforations high in the esophagus have a better prognosis than those lower down. Mörl gave several reasons for this. First, in perforations of the cervical portion of the esophagus, the tendency is for the resultant inflammatory process in the mediastinum to spread upward where it is more easily accessible to surgical intervention. Second, the inflammatory process in the superior mediastinum appears to lead to a more limited process than that resulting from a perforation lower in the esophagus. Finally, the relatively easy accessibility to the site of perforation, not only from the outside but also from within, with the aid of the esophagoscope, makes it less dangerous. The duration of the underlying pathology before the time of perforation also appears to alter the extent of the resultant mediastinitis. In perforations of the esophagus secondary to a long standing process, there is a tendency toward a localized periesophagitis rather than a diffuse mediastinitis. This is apparently due to walling off of the inflammatory process from the fibrosis attending the underlying chronic esophageal lesion. Perforations of the lower esophagus commonly rupture into the pleural cavity, with an invariably fatal outcome. Mörl believed that recovery in these cases belongs to the "great rarities of clinical medicine."

Immediately above the diaphragm the esophagus and mediastinal pleura are in close apposition. Also, this portion of the esophagus has been shown experimentally by Weiss and Mallory (quoted by Eliason and Welty), MacKenzie and Taylor, and Thalheim Brosch and Bencke (quoted by Wagner) to be the weakest, and it is here where under increased pressure from vomiting or coughing, spontaneous perforation occurs and the pleura is most often torn. Numerous authors (Williams and Boyd, Brown, Collis, Humphreys and Bond, Mörl, Eliason and Welty) have reported such cases of esophageal rupture where at autopsy no apparent cause for the perforation could be found. Perforations higher in the esophagus may result from a number of causes.

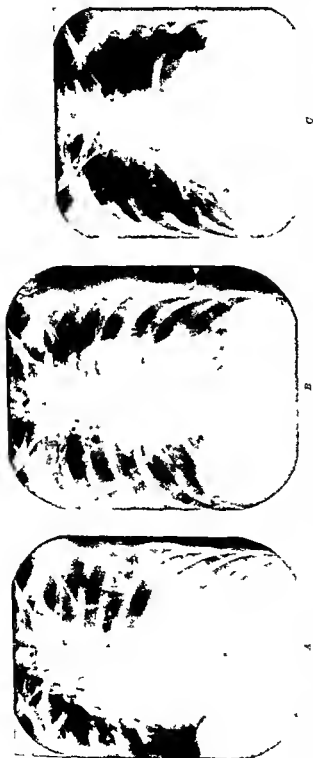


Fig. 3 (Case 3).—A. Roentgenogram made on admission showing a large area of hydro pneumothorax. The return of the mediastinum to normal position can be noted. B. Roentgenogram made the day following admission with suction needle in place. The return of the mediastinum to normal position can be noted. C. Roentgenogram after suction was removed from left side of chest. Again the hydro pneumothorax is under tension and the mediastinum is deviated.

A roentgenogram of the chest and abdomen showed a left hydropneumothorax with practically complete collapse of the lung. The heart and mediastinum were markedly shifted to the right. No free air was demonstrated in the peritoneal cavity. The patient died approximately twelve hours after a laceration.

The autopsy in part revealed a 12 by 0.4 cm. acute perforation in the lower esophagus just above the level of the diaphragm, the perforation opening into the posterior mediastinum and into the left pleural cavity. The left pleural cavity contained about 2 L. of regurgitated gastric content, with particles of vegetable matter being very apparent. The entire mediastinum was markedly shifted to the right and the entire left lung was completely collapsed. There was marked inflammatory edema of the posterior mediastinum with a fair amount of purulent exudate surrounding the esophagus.



FIG 1

FIG 1 (Case 1)—Hemiprism view of the chest. tension hydropneumothorax is readily recognizable.



FIG 2

FIG 2 (Case 2)—Upright view of the chest. tension hydropneumothorax is as noted in Case 1. On the original roentgenogram subcutaneous emphysema in the upper chest could be recognized (more readily) than on this reduction.

CASE 2. The patient was a white man aged 30 years admitted to the Buffalo General Hospital in the morning with a history of occasional epigastric distress (known duodenal ulcer). The previous night he had experienced nausea followed by emesis. Shortly afterward he had sudden sharp pain in the lower part of the chest and pain radiating across the scapulae. On arrival at the hospital the patient was in shock and appeared cyanotic and orthopneic.

A roentgenogram of the chest taken on admission revealed practically complete collapse of the left lung, by a hydropneumothorax fluid level reaching the eighth interspace posteriorly. The heart and mediastinum were shifted to the right. There was also marked subcutaneous emphysema of the neck and upper chest. The patient died that same evening.

The autopsy revealed a perforation in the anterior wall of the stomach.

The ulcer measured 2.5 by 0.7 cm. A second typical chronic ulcer oval shaped and measured 1.5 by 0.5 cm. was situated in the superior aspect of the first portion of the duodenum.

The patient was treated symptomatically and the emphysema and pain lessened. The temperature gradually came down so that by the tenth day it was normal. She was discharged on May 20, 1946, greatly improved.

Three of the four cases presented illustrate rather massive esophageal perforations into the pleural cavity with resultant hydropneumothorax. The fourth case illustrates a perforation high in the esophagus in which the pleura was not involved. The patient experienced a moderately severe mediastinitis from which she recovered.

We feel that the radiographic finding of hydropneumothorax in a patient who experiences sudden onset of chest and/or abdominal pain accompanied by shock and collapse is diagnostic of a perforation of the upper gastrointestinal tract either lower esophagus or stomach into the mediastinum and pleural cavity. Spontaneous pneumothorax should be readily differentiated radiographically from pneumothorax occurring secondary to esophageal perforation by the absence of an associated pleural effusion. The lung following a spontaneous collapse usually re-expands without a complicating effusion; however, if fluid forms it is not until some time after the initial collapse. In cases of esophageal perforation on the other hand the collapse and formation of fluid occur simultaneously.

In reviewing the literature on this subject it was found that when a plain x-ray view of the chest was taken showing a hydropneumothorax it was rarely regarded *per se* as being a *diagnostic criterion* of esophageal perforation but was thought of primarily as confirming the clinical finding of a pulmonary collapse. Many of the cases reported (described later in this paper) showed radiographic evidence of sudden onset of hydropneumothorax; however, the diagnosis of esophageal perforation was not made until sometime later or until after death. In other instances the chest roentgenogram was used as an adjunct for determining the amount of soft tissue swelling and emphysema thereby following the progress of the condition. Fliszen and Welty concluded from their study of the subject that spontaneous rupture of the esophagus is much more common than appreciated and that in most instances the diagnosis is not made until the patient comes to autopsy. This is probably due in part to the varied symptomatology which esophageal perforation presents suggesting coronary occlusion, pulmonary embolism, dissecting aortic aneurysm, spontaneous pneumothorax, acute pancreatitis, gastric perforation or mesenteric thrombosis and furthermore to the fact that it is not thought of in the differential diagnosis when the patient is first seen. One of their cases was definitely diagnosed radiographically before death by the presence of air in the mediastinum.

Friedenwald and Morrison reported three cases of perforation through esophageal carcinomas secondary to instrumentation. One of their patients showed a hydropneumothorax radiographically. They stated that the rapid development of a hydropneumothorax is a 'suggestive sign' of esophageal perforation. Smerd emphasized the mediastinal widening and emphysema as being indicative of a perforation of the esophagus. Collis Humphreys and Bond likewise believed that the most valuable diagnostic signs of esophageal

brown stomach content and *fibrinous exudate* in the mediastinal soft structures particularly surrounding the perforated lesion. The mediastinal parietal pleura of the left chest overlying the site of perforation showed very distinct peptic digestion in an area measuring 3.5 by about 2.5 cm with broad communication between the mediastinum and the left pleural cavity. There was a marked left pneumohydrothorax with between 1,500 and 2,000 cc of fluid and stomach content in the left pleural cavity, including several particles of partially digested food.

CASE 3—The patient, a 47 year old woman, was admitted to the Buffalo General Hospital a few hours after esophageal dilatation with complaints of pain in the left lower part of the chest and epigastric distress. She had complained of dysphagia for approximately one year and esophagoscopy had revealed a mild cardiospasm.

A chest roentgenogram at the bedside revealed marked displacement of the mediastinal structures toward the right, and a left hydropneumothorax.

The patient had a septic course, and fluid aspirated from the left side of the chest shortly after admission resembled ingested liquids. Repeated chest taps subsequently revealed thick, foul, pale yellow exudate. The patient continued a steadily downhill course and died nineteen days after admission.

Serial roentgenograms of the chest showed no appreciable change in the appearance of the left hydropneumothorax. Permission for autopsy was not obtained.



FIG. 4 (Case 4)—A Posteroanterior view made at time of admission showing diffuse mediastinal widening and subcutaneous emphysema in the upper chest. B Repeat view following recovery demonstrating return to normal.

CASE 4—The patient was a 61 year old woman who was admitted to the Brook's Memorial Hospital May 12, 1946, with the complaints of chest pain, difficulty in breathing and swallowing, and pain in the abdomen. Temperature on admission was 102.4° F, rectal pulse 130, and respiration 35.

The patient had been esophagoscoped the previous day for unexplained difficulty in swallowing. She was extremely uncooperative during the procedure which was carried out with difficulty under local anesthesia.

Physical examination at time of admission revealed rather marked subcutaneous emphysema involving the neck. A roentgenogram of the chest showed diffuse widening of the mediastinum, apparently resulting from a diffuse mediastinitis. The pulmonary fields revealed a linear area of fibrosis just above the left diaphragm otherwise nothing unusual.

until gastric contents were subsequently removed from the right pleural cavity. The patient died within forty eight hours from the time of the accident.

Several of the authors cited have given contrast media by mouth in order to visualize the communication between the esophagus and pleural cavity. Smead agreed that it is an impractical and hazardous procedure. Mori stated that the demonstration of the perforation by oral barium is undesirable in the active stage because of the condition of the patient. He believed it to be indicated, however, if the patients have withstood the perforation for several days. He qualified this statement by saying, "if care is taken to give only small portions of barium, then the patient can certainly not be harmed, but the experiment may clear up many a pathologic relationship and give indications for further therapy." In two of Wagner's patients, contrast media was given and in each it was seen under the fluoroscope to pass into the main stem bronchus. Berger (quoted by Wagner) reported a case of death by asphyxia shortly after the administration of barium by mouth.

In the patients who withstand the perforation, the upper or cervical portion of the esophagus is usually the seat of the perforation, and the pleural cavity is not secondarily involved. It is in these patients that barium may be given by mouth to substantiate the diagnosis. Where there is marked pleural involvement, indicative of a perforation lower in the esophagus with a free communication between the esophagus and pleural cavity, it is undesirable for obvious reasons to give contrast media by mouth. We believe that the scout chest x ray view offers one of the best criteria for a diagnosis in these cases and that the administration of contrast media would be of academic interest only.

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perforation are the deep emphysema in the neck and physical findings indicating fluid or air in the chest. These signs according to these authors together with the radiographic evidence of a mediastinitis in a patient who experiences a sudden onset suggesting a perforated peptic ulcer coronary occlusion or spontaneous pneumothorax should confirm the diagnosis.

Ballin and Saltzstein reported a case of perforation into the pleural cavity which was thought at first to be a gastric perforation because of the abdominal and diaphragmatic rigidity and the respiratory distress. An abdominal laparotomy however was negative. The patient subsequently died, and a large left hydrothorax and a perforation of the esophagus into the left pleural cavity secondary to an ulcer two inches above the diaphragm were found at autopsy. No roentgenograms of the chest were taken. Benson and Penberthy reported a case of esophageal perforation secondary to an ulcer in a child of 2 years of age with recovery. The patient had been esophagoscoped four hours previously. A plain x-ray view of the chest showed a tension pneumothorax with pleural effusion. These authors concluded that together with the knowledge that the ulcer existed the finding of the hydro-pneumothorax strongly suggested esophageal perforation.

In the case reported by Wallfield the perforation was not suspected despite the radiographic finding of a hydro-pneumothorax until after yeast and *Bacillus acidophilus* were recovered from the pleural fluid. Subsequent fluoroscopic examination during the ingestion of iodized poppy seed oil showed a communication of the lower esophagus with the right pleural cavity. The patient presented a vague history of having swallowed a chicken bone three weeks prior to death (the day of onset of symptoms). Gott concluded from four cases he observed that a sudden onset of pain in the lower part of the chest coming on during vomiting and associated with hematemesis subcutaneous emphysema of the neck respiratory distress and prostration are pathognomonic of esophageal rupture. One of his patients was x-rayed and showed a hydro-pneumothorax. All four showed hydro-pneumothorax at autopsy.

Baumeriellie in his excellent article on pleural manifestations in esophageal perforations stressed pleuropulmonary manifestations as being an important diagnostic sign of esophageal perforation in patients who present a history of swallowing a foreign body or caustic fluid. In the majority of cases studied by this author the pleura became involved and it is the pleural complications in particular that suggest perforation of the esophagus. In Roszak's case the diagnosis was not made until after gastric contents were removed from the left pleural cavity. A subsequent chest roentgenogram confirmed the presence of a left hydro-pneumothorax.

Aldrick and Anspach reported an interesting case of esophageal perforation in a 6 month old child as a result of a blow to the upper abdomen from a fall. A x-ray view of the chest taken eight hours after the accident showed a right pneumothorax. The second view of the chest taken the second day revealed a massive right pleural effusion. Despite this radiographic evidence its full significance was not realized and the perforation was not suspected.

TABLE I. DIVISION INTO DIFFERENT TYPES OF VOLVULUS

TYPE OF VOLVULUS	PETERSON FINLAND	ECKEN FINLAND	LAUFFEL SWEDEN	TIIOINEN FINLAND	ULLEVAAL DEPT II & III
Cecum	105	7	1	17	7
Transverse colon	1		3	1	4
Sigmoid colon	128	14	26	23	91

more about and a beginning volvulus in women has a greater possibility of spontaneous reduction. Of the patients in Peterson's study 86 per cent were men, in Ullevaal 61 per cent were men.

ETIOLOGY

Conditions Predisposing to Volvulus of the Sigmoid

1. A long and freely movable sigmoid colon. An increase in length of the sigmoid colon may be caused by chronic constipation, volvulus attacks of a passing nature spontaneously repaired or kink torsion. A diet high in vegetables and residue such as is common in eastern European countries and in countries on war rations is a contributing cause of volvulus of the sigmoid.

2. A long and freely movable mesosigmoid.

3. A sigmoid loop whose limbs lie close together. This condition is present in a mesosigmoid with a small fixation angle to the posterior abdominal wall and is also caused by shrinking mesosigmoiditis which is probably the result of previous attacks of volvulus, constipation or possibly diverticulitis. In the Ullevaal study sixteen of the eighteen patients operated upon or examined post mortem had shrinking mesosigmoiditis.

The location of the sigmoid colon varies with the amount and weight of contents and the position of the body. The most moderate form of volvulus of the sigmoid is a clockwise torsion of 180 degrees described by Wilms as physiologic volvulus. This is not usually accompanied by intestinal symptoms and x-ray examination shows that it usually repairs itself spontaneously without any sign of obstruction of the bowel or disturbance of circulation. In 180 degree counterclockwise torsion of the sigmoid the proximal sigmoid loop may be squeezed between the distal scybal-filled sigmoid loop and the posterior abdominal wall causing obstruction and a circulatory disturbance in the sigmoid flexure.

PATHOGENESIS

Wilms believed that volvulus which causes symptoms develops from the symptom-free 180 degree physiologic volvulus in most cases. The rectal loop which lies behind the colonic loop may be gradually filled with gas and stool because of retention. The heavy rectal loop then changes its position and falls in front of the empty colonic loop, possibly as a result of a movement of the body to the right. Thus torsion of 360 degrees is accomplished.

The intensity of the occlusion and strangulation increases with the increased degree of torsion but it is chiefly as a result of tension and limitation of the torsion site that complete occlusion and strangulation occur. Volvulus of more

VOLVULUS OF THE SIGMOID COLON AND ITS TREATMENT

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DEFINITION

CLINICALLY speaking the term volvulus means a torsion of the bowel on its mesentery which cause symptoms, whether the symptoms are caused by narrowing of the bowel, strangulation of the blood vessels, or both (Laurell). This definition includes not only volvulus with an acute course but subacute and chronic cases as well.

OCCURRENCE

According to statistical studies, volvulus of the intestinal tract accounts for 30 to 50 per cent of the intestinal obstructions in the eastern European countries (Finland, Russia, the Baltic States and others). In western European countries and the United States volvulus makes up about 10 per cent of the total intestinal obstructions.

The presence of a movable mesentery to give the bowel mobility is a prerequisite for volvulus. Therefore, volvulus is localized in the stomach, small bowel, cecum, transverse or sigmoid colon, but not in the retroperitoneal parts of the bowel.

LOCALIZATION

In large statistics, volvulus of the small bowel usually makes up 25 to 30 per cent of the entire number of volvulus cases. In his study of 230 cases the Finnish surgeon Lennart Peterson found that volvulus of the small bowel made up 24 per cent.

Volvulus of the large bowel is the most common. In most cases the site of the lesion is in the sigmoid colon.

The Ullevaal study of volvulus of the sigmoid which includes cases from Department II and Department III shows a marked increase in the number of patients treated during the war years that is 85 of the patients were treated after September, 1939.

AGE AND SEX DISTRIBUTION

Volvulus of the sigmoid is seen rarely in individuals under 30 years of age. Among the ninety-one cases mentioned in Table I under the Ullevaal heading, there were only four patients under 40 years of age while fifty-seven were over 60 years. Volvulus occurs more often in men than in women because the female pelvis is wider and the abdominal wall particularly after pregnancies, is more relaxed. Therefore, the loops of the bowel have more room to

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2. A long and freely movable mesosigmoid.

3. A sigmoid loop whose limbs lie close together. This condition is present in a mesosigmoid with a small fixation angle to the posterior abdominal wall, and is also caused by shrinking mesosigmoiditis which is probably the result of previous attacks of volvulus, constipation or possibly diverticulitis. In the Ullfvaal study sixteen of the eighteen patients operated upon or examined post mortem had shrinking mesosigmoiditis.

The location of the sigmoid colon varies with the amount and weight of contents and the position of the body. The most moderate form of volvulus of the sigmoid is a clockwise torsion of 180 degrees, described by Wilms as physiologic volvulus. This is not usually accompanied by intestinal symptoms and x-ray examination shows that it usually repairs itself spontaneously without any sign of obstruction of the bowel or disturbance of circulation. In 180 degree counterclockwise torsion of the sigmoid the proximal sigmoid loop may be squeezed between the distal scybal-filled sigmoid loop and the posterior abdominal wall causing obstruction and a circulatory disturbance in the sigmoid flexure.

PATHOGENESIS

Wilms believed that volvulus which causes symptoms develops from the symptom-free 180 degree physiologic volvulus in most cases. The rectal loop which lies behind the colonic loop may be gradually filled with gas and stool because of retention. The heavy rectal loop then changes its position and falls in front of the emptier colonic loop, possibly as a result of a movement of the body to the right. Thus torsion of 360 degrees is accomplished.

The intensity of the occlusion and strangulation increases with the increased degree of torsion but it is chiefly as a result of tension and limitation of the torsion site that complete occlusion and strangulation occur. Volvulus of more

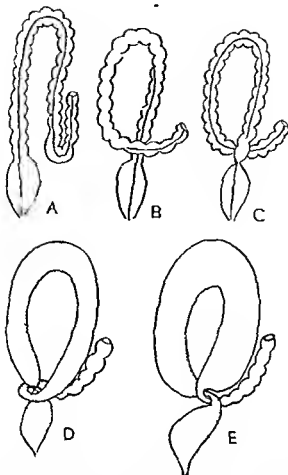


Fig 1—A Long sigmoid. B phy alone vol ulus. C axial torsion of the rectal loop of the sigmoid in 180 degree volvulus without strangulation of the vessels. D 180 degree volvulus of the sigmoid with beginning strangulation. E 360 degree volvulus of the sigmoid with torsion and strangulation.

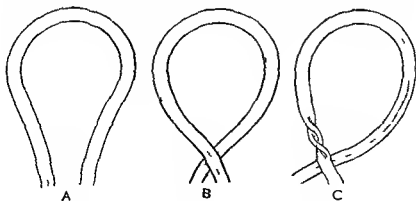


Fig 2.—Development of torsion stenosis. (From Laurell.)

than 360 degrees is comparatively rare because a torsion of 360 degrees causes so marked a distension of the flexure that it limits itself and further twisting becomes impossible

Seventeen of the Ullevaal patients operated upon or examined post mortem showed the degrees of torsion listed in Table II

TABLE II

NUMBER OF CASES	DEGREES
1	540
6	360
1	270
9	180

Hugo Laurell's assistant Karl E. Groth has demonstrated a condition characteristic of a volvulus which produces symptoms particularly when there is a moderate twisting of the mesentery that is, volvulus of approximately 180 degrees

Groth showed that every torsion of the sigmoid and its mesenteric axis is combined with an axial torsion of the bowel itself because the end of the sigmoid is more or less fixed to the posterior peritoneal wall. This axial torsion is twice as great as the torsion of the mesentery. The axial torsion is thus 360 degrees in a 180 degree volvulus. To what extent the axial torsion causes stenosis depends on whether it is evenly distributed throughout the entire sigmoid flexure or is limited to one or more short lengths of the loop. A stenosis of the type designated by Laurell as torsion stenosis occurs where the torsion is concentrated at the points of attachment of the loop particularly where part or all of the torsion is localized at one side of the loop's vertex. This takes place when the twisted loop is distended with gas. Axial torsion then is forced along until it comes to a fixed part of the bowel. A kink torsion may occur if there is unequal filling of the sigmoid flexure.

The twisting at the axis of the mesentery and the axial torsion about the axis of the bowel which are characteristic of volvulus cause a mechanical ileus in most cases. In those cases in which the torsion is moderate a simple obstruction results. The most important pathologic changes are then caused by distention of the bowel and obstruction. The increased peristalsis seen in these patients forces air and fluid into the twisted sigmoid loop because the site of the torsion acts as a valve which allows air to enter but not to escape. This explains the rapidly developing meteorism in the sigmoid loop. Occasionally the bowel contents may be forced into the efferent loop so that diarrhea may occur in spite of the other symptoms of occlusion.

When volvulus causes a simple obstruction the bowel wall remains adequately nourished for the first few days. This is a result of the fact that the sigmoid colon is the part of the intestinal tract that tolerates the highest pressure before blood circulation in the wall stops and therefore is most resistant to the increasing intestinal pressure. Investigators seek the cause of this condition in the different courses of the vessels in the muscular wall in the different parts of the intestinal tract.

At operation during the early stages the serosa of the sigmoid is found to be smooth and glistening and the mucous membrane does not show evidence of any ulceration. In the later stages these cases also show damaged mucous membrane with ulceration and perforation as a result of the torsion and disturbed circulation.

The situation is more serious in the cases in which the volvulus produces a strangulation ileus. As the strangulation increases the veins are increasingly closed off, and venous stasis occurs. The changes found in the bowel are in direct proportion to the degree of disturbance in the circulation. Sooner or later, depending on the degree of the torsion, thrombosis of the mesentery sets in and spreads. The strangulated loop becomes gangrenous, capillary or larger perforations occur, and peritonitis develops. Usually three or four days elapse before the infarction of the bowel wall becomes so marked that peritonitis develops, but in the most marked strangulations in which the arteries are occluded a much more rapid development of the pathologic changes may be seen. It is important to bear in mind the changes which take place at the site of torsion. In volvulus with simple obstruction these are more marked at the site of torsion than are the changes seen in the remainder of the sigmoid loop.

After the detorsion of the sigmoid colon perforation at the site of the torsion may occur and have a fatal outcome. Increased peristalsis, meteorism and accumulation of fluid soon appear in the prestenotic loop of the colon. Distention is most marked where there is a "closed loop" that is in instances in which the ileocecal sphincter functions. Exudation in the peritoneal cavity is common in volvulus of the sigmoid flexure. In the Ulleval study this was found at x-ray examination in two thirds of the cases. The exudate is yellow and serous in cases of obstruction. Peritoneal exudate with a fecal odor is a sign of grave changes in the sigmoid loop. In volvulus of the sigmoid with a functioning ileocecal valve the small bowel continues to have normal function for some time and the fluid and electrolyte losses are therefore moderate. In more serious forms of volvulus there is fluid and electrolyte loss resulting from formation of ascites, hemorrhage and vomiting.

THE DISEASE HISTORY

The disease history in volvulus of the sigmoid has several characteristic symptoms which may be explained on the basis of pathologic changes. The first and most important point is the change from normal bowel evacuation, usually a long continued or periodic constipation. The stools may be bloody or, at times, foul smelling. A report of passing attacks of acute abdominal pain is common. After several milder attacks the patient suddenly has a severe acute attack which makes hospitalization necessary.

A volvulus attack that brings the patient into a hospital may show great variation in its initial symptoms. Some patients report that for several weeks previous to the attack they have noticed a marked decrease in passage of stool and flatus simultaneous with increasing gaseous distention of the abdomen. In other cases the patient may notice a marked sudden stoppage of stool and

flatus, but aside from a noticeable desire for evacuation which he cannot satisfy, one or more days may pass before he has severe symptoms from the sigmoid volvulus, mainly pain, which brings him to the physician.

There are also patients who report milder cramping pain often localized around the umbilicus and accompanied by rumbling in the abdomen and some times liquid stools. The intensity of the pain increases rapidly after the onset as a rule.



Fig. 3.—Characteristic contours of the rectum in torsion stenosis.

The number of days from the onset of the symptoms to the admission into the hospital was quite variable in the Ullevaal study. In most cases the patients reported having had symptoms from twelve to seventy-two hours, but in a few cases the duration of the symptoms was as long as ten days or more. A few patients reported that they had not noticed any cessation in the passage of flatus or stool.

As a whole the patients with volvulus of the sigmoid on admission to the hospital appeared less affected than patients with ileus from other causes. Among the 91 patients admitted to Ullevaal a total of 168 times, there were only 21 admissions in which the general condition of the patient was poor. However, patients with acute marked strangulation may present a picture of

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- 7 Thickened but smooth walls in the sigmoid flexure
- 8 Domes of the diaphragm high and almost rigid
- 9 Fluid in the peritoneal cavity This occurred with progressive compromise of the circulation of the torsioned sigmoid
- 10 Signs of peritonitis in strangulation with gangrene as suggested in the presence of fluid between the distended intestinal coils
- 11 Barium enema demonstrating a characteristic outline of the proximal part of the rectum a bird's bill shape with spiral narrowing The sharply cut off margin as is observed in cancer is never seen in volvulus

In atypical cases the diagnosis is difficult and the examiner may make mistakes. An x ray check on the effect of treatment is of the greatest aid.

TREATMENT

The treatment may be either nonoperative or operative. There is a possibility that spontaneous untwisting of the sigmoid exists when the torsion is less than 360 degrees. In torsion of 360 degrees or more the twisted loop is usually held fast between the anterior and posterior abdominal wall.

In the Ullevaal study the volvulus condition was repaired spontaneously in only three cases after the patient was admitted to the hospital. Many of the case histories suggest that a spontaneous reposition of the volvulus is common. However it is difficult to determine when the conditions for such repair are present. An ordinary enema may be followed by detorsion if the degree of torsion is moderate. The effect is often uncertain and temporary and it is difficult to be certain that the volvulus has been completely untwisted. In the Ullevaal study detorsion occurred twice after an ordinary enema. A better and more easily controlled method is an attempt at reposition by means of a barium enema during fluoroscopy. Norgaard has described successful reposition by this method. It was not used routinely at the Ullevaal but volvulus was twice repaired during examination with a barium enema.

The chief obstacle to reduction of the torsioned and distended sigmoid loop is that the loop usually fastens itself because of its size thus hindering the bowel's own attempt at untwisting. It is reasonable to suppose that a spontaneous reduction could take place if one emptied the bowel. The axial torsion would not then be forced into a limited part of the sigmoid but could be divided over a larger area thus allowing spontaneous detorsion to take place. A number of investigators have described the immediate detorsion of the volvulus which takes place when a tube is inserted past the site of the torsion. The prerequisite for carrying out such treatment consisting of inserting a tube or other hollow instrument past the site of torsion is that there is no danger of injury particularly of perforation at the site of torsion. This latter method has been used in the treatment of volvulus of the sigmoid at Ullevaal hospital in most cases with good results as I shall relate later.

The simplest means of emptying the sigmoid flexure is to insert a tube per rectum past the stricture. This method has some drawbacks. It is necessary

deep shock in the course of the first day of the disease. Three of the Ullevaal patients died during the first day of the attack. Post mortem examination in these patients showed marked gangrene of the sigmoid loop.

The acute pain is characteristic of volvulus. The pain is continuous in indicating a pull on the mesentery but it is interrupted by colicky pain which is the result of hyperperistalsis. The pains are diffuse without radiation but they have a tendency to be most marked round the umbilicus.

Inspection of the abdomen shows balloonlike distention localized chiefly to the epigastrium umbilical region and left hypochondrium. The outline of the loops may often be seen. It is noteworthy that in the large number of cases in the Ullevaal study only four patients were described as having an abdomen with a normal appearing contour. In seven cases the abdomen was described as somewhat distended while in the remainder of the cases there was marked distention which thus is seen to be a fairly constant symptom of volvulus of the sigmoid. Auscultation of the abdomen is of great importance. Except in enteritis fluid sounds (gurgle sounds) are a constant finding in ileus. They were found in almost all cases in the Ullevaal study of volvulus of the sigmoid. Marked tenderness and muscular resistance are rare and are symptomatic of a bowel lesion with peritonitis. Vomiting occurs as a reflex at the onset but later vomiting is rare and indicates complications. Digital examination of the rectum shows a large empty ampulla. The site of the torsion is too high for palpation per rectum but occasionally a certain amount of resistance can be felt. Fever occurs only in complicated cases. Laboratory examinations required for the necessary supportive treatment are in order but such examinations do not offer any special help in diagnosis.

X RAY EXAMINATION

The x ray examination which is of great importance in both diagnosis and treatment should be done in all cases in which there is a suspicion of volvulus. This was carried out routinely by the x ray department at Ullevaal.

X rays of acute volvulus of the sigmoid reveal some of the following findings:

- 1 A more or less markedly distended sigmoid.
- 2 Fluid levels in the sigmoid loop with little difference in levels in erect position. (This symptom was absent in one of sixty patients examined the last years at Ullevaal.)
- 3 Moderate gaseous and fluid distention of the remainder of the colon. (Absent in one of our sixty cases.)
- 4 Balloonlike distention of the cecum rare and seen chiefly in peritonitis. (Such distention was observed in one of our sixty cases.)
- 5 Gas in the small bowel rare and seen chiefly in peritonitis. (It was found in nine of the sixty cases.)
- 6 Spiral patterns on the mucous membrane at the site of torsion. This occurred only when the torsion was limited to a small segment of the bowel.

is a strong argument against such warning. That such warning cannot be entirely ignored should be an added incentive for caution to those using the method. The method must not be used when the clinical examination leaves some doubt as to whether there are serious circulatory changes in the bowel either at the site of torsion or elsewhere.

In one case the bowel was perforated during insertion of the tube after proctoscopy. A laparotomy was done but the patient, a 71 year old man, died. Three patients died in spite of treatment with proctoscopy and intubation of the obstructed sigmoid but not because of the treatment. All three patients were in poor condition upon admission and died after a few days. No signs of volvulus of the sigmoid or gangrene were found at the post mortem examination.

Proctoscopy and attempts at intubation were unsuccessful nine times. These patients were operated upon immediately afterwards. The previous treatment had no untoward effect in so far as could be determined. In a very few patients the method was not used because clinical and x ray findings contraindicated its use. Two patients were in such poor condition at the time of admission that they died about one half hour after arrival before any treatment was begun.

This treatment should perhaps be credited with a fatality in one case in which there was no volvulus. The patient was an 80 year old man who was treated with proctoscopy and intubation after the condition was diagnosed as volvulus of the sigmoid. When the treatment failed to produce the desired effect and because of the onset of symptoms of peritoneal irritation laparotomy was performed the next day. The distal part of the sigmoid was found to be constricted by a strangulating band. There was no perforation and no volvulus. Division with closure of the distal segment of the sigmoid and exteriorization of the proximal part was done. The patient died of an intra peritoneal hemorrhage the next day.

A mortality of 4 in 136 treatments is to be considered a satisfactory result. The drawback of the method is that it is not a definitive treatment. The tendency to recurrence is great and these patients are in and out of the hospital many times in the course of a few years. Thirty one of the 115 colic patients were admitted to the department two or more times for the disease. However they are older people many of them aged who run a considerable risk from radical operative treatment.

OPERATIVE TREATMENT

In the cases in which treatment with proctoscopy and passage of a tube could not be done, serious bowel damage could not be ruled out or in which the treatment was not successful laparotomy was done. The simplest and according to our experience correct operative procedure is laparotomy accompanied by insertion of a tube per rectum and detorsion. In order to do this safely there must be no gangrene at the site of torsion nor any other serious bowel damage. I believe it is correct to insert a tube controlling its passage by placing a hand in the peritoneal cavity as soon as the abdomen is opened.

to use a fairly soft tube to avoid the danger of perforation and a soft tube may easily curl back upon itself instead of passing the site of occlusion because it would be only the merest chance that a tube could find its way past the obstruction.

In the Ullevaal study reduction by means of a tube was accomplished in five cases with good results. Some patients have employed such treatment themselves. A 64 year-old man reported that in the course of the last twenty years he had regularly used a tube 7 mm. in diameter and 60 cm. long as soon as he noticed any distention. In this way he relieved both the distention and the pain at least once a week and sometimes daily.

Experience has shown that it is much easier to guide the tube past the point of torsion if it is inserted through a proctoscope so that the field may be seen. After the surgeon has been informed by the roentgenologist as to the degree of occlusion and the direction of the bowel he may insert the proctoscope as far as the site of torsion with the aid of careful inflation of the rectum. The site is easily recognized by the spiral folds seen there. Proctoscopic examination provides the examiner with an impression of the condition of the bowel, the appearance of the mucous membrane and the blood supply at the site of torsion. In some cases the appearance of the mucous membrane may be such that the examiner considers it risky to insert the tube.

When the site of torsion has been located a lubricated rubber rectal tube 60 cm. long and about the thickness of a finger is guided up past the site of obstruction. Force must not be used but the tube usually slips into place without trouble. In some cases the proctoscope has been inserted past the site of torsion before passing the tube but the method first described is considered the best. There is very seldom doubt whether the treatment has succeeded because a forceful evacuation of flatus and thin stool is immediate and the patient feels instant relief. The result may be verified by x-ray examination.

Usually the torsion of the sigmoid is between 15 and 20 cm. from the anus. In the Ullevaal study the proctoscope was inserted more than 30 cm. before coming to the site of torsion in only six cases. At Ullevaal where proctoscopy with the use of the tube has been the routine method of treatment for volvulus of the sigmoid for several years the method was followed by an immediate satisfactory result in a total of 123 trials in the period from 1936 to 1946.

In judging the reduction of the volvulus by this means as satisfactory there is one reservation necessary, that although the method is effective in the treatment of the acute attack it has no effect on the marked tendency to recurrence. This tendency was not infrequent among the patients referred to previously. When the tube slipped out soon after the reduction of the volvulus recurrence was noted within a few hours in some patients. Therefore it is necessary that the tube remain in place two or three days after reduction. The tube should be sewn to the anal ring. The patient should be observed very closely the first few days after the treatment.

I have heard surgeons warn against the method which I have just discussed because of the danger of perforation and because one might fail to operate on patients with strangulation and gangrene. I believe that the Ullevaal study

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and to delay the risky reposition of the distended sigmoid flexure until the flatus and fluid have been removed. If there is gangrene the loop should be lifted out of the peritoneal cavity and punctured. In the cases in which there is gangrene of the sigmoid loop bowel resection should be done.

Because the site of torsion is so distal in the sigmoid flexure a Mikulicz exteriorization resection cannot be employed in most instances because there is some risk of producing too much pull on the efferent loop of the sigmoid colon which may cause gangrene and peritonitis. The operative treatment should be carried out in such a manner that after resection of the gangrenous part of the sigmoid the distal stump is inverted and buried. Then the proximal part is brought out as a colostomy opening. An anastomosis between the proximal and distal parts of the sigmoid may be made at a later laparotomy.

Eighteen patients were operated upon during the acute stage in the Ulevaal stink. Ten patients were treated with laparotomy and detorsion. One of the latter died as the result of peritonitis which developed from a distention perforation of the rectum. One patient had a primary resection of the colon with a satisfactory result. One patient had a sigmoidostomy with a satisfactory result. One patient was treated with eecostomy after a wrong diagnosis of cancer of the sigmoid was made. This patient did not have x-ray examination with a barium enema because the roentgenologist thought the risk was too great. The patient died.

Sigmoidostomy and eecostomy have no place in the treatment of volvulus of the sigmoid. Resection of the sigmoid colon with exteriorization by the method of Mikulicz was done in five cases. One of these patients was referred to before. In this case perforation occurred after insertion of the tube. In two cases pneumoperitoneum and peritonitis resulting from perforation of gangrenous bowel loop were found at operation. The fourth patient an 87 year old man was found to have a completely gangrenous sigmoid flexure. All these patients died. The fifth patient did not die as the result of the exteriorization resection but in connection with the closure of the sigmoid fistula.

RESULTS OF CONSERVATIVE AND OPERATIVE REDUCTION

The collected results of the treatment of acute volvulus of the sigmoid at the surgical departments of Ulevaal Hospital give the figures listed in Table III.

TABLE III

KIND OF TREATMENT	NUMBER OF TREATMENTS	DIED
None	2	2
Spontaneous reduction	—	—
Reduction by enema	—	—
Reduction with a laxative	—	—
Reduction with a rectal tube	—	—
Reduction with proctoscopy and irrigation	1	4
Laparotomy and detorsion	11	1
Laparotomy and eecostomy	1	1
Laparotomy and sigmoidostomy	1	—
Laparotomy and primary resection	1	—
Laparotomy and exteriorization resection	3	5
Total	18	11

The mortality rate for the 168 treatments is thus 77 per cent. The mortality rate for the 91 patients treated is 14.2 per cent. This is a satisfactory rate considering the circumstance that most of the patients were old, many exhibiting the mental deterioration accompanying senility. Moreover, the physical condition of many of the patients was poor.

From many clinics in which operative treatment is used exclusively, the mortality rate is reported to be as high as 30 to 60 per cent. Radical removal of the sigmoid which has undergone repeated torsions may be carried out with small fatal risk during the symptom-free interval. At Ullevål Surgical Department III the method used was resection of the enlarged sigmoid loop in several stages: (1) cecostomy, (2) exteriorization, (3) fixation by the Mikulicz



Fig. 4.—Volvulus of the sigmoid before and after reduction with proctoscopy and intubation. (From the records of the Minnesota Hospitals.)

method, (3) closure of the sigmoidostomy, (4) closure of the cecostomy. In the ten-year period from 1936 to 1946 this procedure was carried out seven times. The results were satisfactory in all cases. Thus, four-stage operation will in most cases keep the patient in the hospital for three to four months.

During my stay at the Minnesota University Hospitals from January to May 1947 I had the opportunity to see two cases of volvulus of the sigmoid reduced with proctoscopy and intubation. In two patients Wangensteen performed a primary resection of the sigmoid about fourteen days after the acute volvulus had been reduced. Both patients were discharged from the hospital in good condition about one week after the operation. In treating patients with repeated attacks of volvulus in the free period of the disease, a closed resection

ACUTE DIVERTICULITIS OF THE CECUM

STUDY OF NINETY NINE SURGICAL CASES

LEO ANDERSON, M D, ROCHESTER, MINN

(From the Division of Surgery Mayo Clinic)

DIVERTICULA of the cecum are usually considered rare Ochsner and Bagen reviewed 151 cases of uncomplicated diverticulosis of the colon and found that in about 2 per cent of the cases the diverticula occurred in the right half of the colon When diverticula or outpouchings occur in the intestine without inflammation the term diverticulosis is applied while if inflammation with or without obstruction occurs the term diverticulitis is used

The incidence of diverticula of the colon in the general population is difficult to evaluate In 31 838 roentgenologic examinations of the colon done at the Mayo Clinic it was found that 57 per cent of the patients examined had colonic diverticula However in 69 per cent of cases in which necropsy was performed during one year at the clinic diverticula of the large bowel were observed

The incidence of diverticulitis is also difficult to evaluate Ochsner and Bagen stated that about 14 per cent of diverticula become inflamed In about 15 per cent of cases of diverticulitis operation is performed

Although diverticula may be found in any portion of the large bowel between the ileocecal valve and the rectum the sigmoid is the most common site The reason for this fact is not entirely clear but the distribution of diverticula may be due to the difference in the consistency of the fecal column In the right portion of the colon it is liquid but in the left portion its formed solid nature makes it possible for fecaliths to exert pressure on the potential hernial areas At these points blood vessels pierce the muscular coat of the intestinal wall and thus leave weakened sites where the mucosa by protruding through may form so called false diverticula

In many discussions of diverticulitis a clear distinction between acute and chronic diverticulitis is not made For our purposes we shall consider that cases in which there were symptoms of sufficient severity to cause operation to be performed coupled with the finding of enough pathologic changes in a cecal diverticulum to explain those symptoms are cases of acute diverticulitis of the cecum

We were unable to find any articles giving a complete review of the literature on acute diverticulitis of the cecum In 1937 Bennett Jones² reported twenty cases from the English literature Five years later Busch and Friedfeld³ reviewed a total of twenty seven cases while adding a case of their own In 1943 Baker and Carlile⁴ summarized thirty seven cases and added two from their own experience

We were able to find in the literature reports of ninety-one cases of acute diverticulitis of the cecum. Of some 700 cases of surgical diverticulitis of the colon at the Mayo Clinic, only nine seemed to be relatively acute surgical problems involving the cecum only.

REPORT OF CASES FROM MAYO CLINIC

CASE 1.—The patient was a girl, 16 years of age. Five days before coming to the clinic she had complained of generalized abdominal cramps, vomiting, and fever. On examination she seemed to have a fullness in the right iliac fossa. Five days after admission to the hospital, as it was felt that the abscess was localized, it was surgically drained. The appendix was not removed. Two split rubber tubes were inserted for drainage. The patient was dismissed from the hospital in twenty-four days, at which time drainage persisted. Three months later the appendix was removed and a large opening in the cecum, which seemed to connect with the fistula, was closed. The patient was dismissed from the hospital in fifteen days. The fistula persisted for one and one-half years and then closed spontaneously. Twenty years after the original visit the patient returned to the clinic complaining of a tender scar, especially so in the past two months. During this time she complained of pain and swelling in the region of the scar, which she could partially relieve by pressure over the swelling. Operation was advised and at exploration an inflamed diverticulum of the cecum, containing a large fecalith, was found, extending up to the undersurface of the anterior abdominal wall. It was possible to free the adhesions about the neck of the diverticulum and invaginate the entire sac into the lumen of the cecum. The base was closed with two rows of sutures. The incision healed without incident and the patient was dismissed from the hospital on the twelfth postoperative day. She returned to the clinic fourteen years after this last operation, or thirty-four years after the first operation, with no complaints relative to the gastrointestinal tract.

CASE 2.—The patient was a woman, 30 years of age. For eight years before coming to the clinic, she had been having intermittent attacks of pain in the right lower quadrant of the abdomen. These attacks had become more frequent in the past year, the last one starting forty-eight hours before admission. Constipation and flatulence were always associated with the attacks. On examination there was observed a tender movable mass about 7 cm. in diameter in the lower right quadrant of the abdomen, which seemed to be contiguous to the right adnexa. At operation, the right ovary and tube were found to be involved in a mass which was attached to an inflamed diverticulum of the cecum. The diverticulum was about $1\frac{1}{2}$ inches (3.8 cm.) in length and was situated about $1\frac{1}{2}$ inches (3.8 cm.) from the base of the appendix. Right salpingo-oophorectomy, appendectomy, and diverticulectomy were performed, the entire mass being removed together. The opening into the cecum was closed with linen sutures. The patient was dismissed from the hospital on the seventeenth postoperative day. She returned to the clinic eight months later. At this time she felt well.

CASE 3.—The patient was a woman 21 years of age. Eight years previous to admission to the clinic, she had had an attack of pain in the right lower quadrant and the appendix had been removed. In the intervening eight years she had suffered from a stabbing pain in the region of the wound and soreness there from time to time. Six weeks before admission well-marked persistent leucorrhea, associated with daily morning diarrhea, had developed. On examination there were considerable thickening and tenderness of the ascending colon. The patient was not inclined to undergo further examination and left the clinic.

Eight months later she returned, having been ill for four days. Temperature was slightly elevated and the abdominal wall over the right iliac fossa was exquisitely tender. The tenderness was perceptible by both rectal and vaginal examination and a small mass was palpable near the cecum. She stated that "pus" had been draining from the rectum in the previous few days. Because of the relatively acute nature of the case, operation

was performed immediately. The uterus was found to be retroverted but the tubes and ovaries seemed normal. There was an inflamed diverticulum, measuring 2 by 4 cm., near the base of the old appendical scar, around which there were many adhesions. It was freed and inverted into the cecum and the base was closed with two rows of chromic catgut. The incision was closed without drainage and the patient was dismissed from the hospital in two weeks. She was seen at the clinic five years later complaining of asthmatic bronchitis. There was no reference to any intra abdominal trouble.

CASE 4—The patient was a woman, 40 years of age. She stated that two years before coming to the clinic, she had had a pelvic operation in which a cystic mass, interpreted as ovarian in origin, had been drained. The incision had never completely healed. She stated that there was daily discharge from a small sinus but that it was not foul or fecal in nature. Five days previous to coming to the clinic she had become ill with nausea, vomiting, and obstipation. The right lower quadrant of the abdomen had been very painful. She was sent directly to the hospital and, when examined there, was found to have a draining sinus from an old lower midline scar, with an egg sized mass just above the inguinal ligament, which was very tender. Leucocytes numbered 9,900 per cubic millimeter of blood. The preoperative diagnosis was draining abdominal sinus with possible adjacent abscess.

Using a secondary midline incision, the sinus tract was dissected down to a region between a small cystic right ovary and a large inflamed diverticulum of the cecum both surrounded by a mass of adhesions and lying in a matted mass of small bowel. The organs were partially separated and the diverticulum was freed at its base, ligated, and cut. The base was inverted into the lumen of the cecum and closed with a purse string suture. Subtotal hysterectomy, right salpingo oophorectomy, and diverticulectomy were performed, the whole being removed in one mass.

Unfortunately, the abdominal sinus persisted and a secondary operation was necessary six months later, at which time the sinus tract was successfully removed. The patient has since remained well.

CASE 5—The patient was a man, 44 years of age. Shortly before he came to the clinic, severe bronchitis and numerous bouts of severe coughing developed. About ten days before coming, he awoke one night coughing severely and noted that the abdomen was greatly distended and that there was considerable distress in the right lower quadrant. When he visited his physician a mass was found in the right lower quadrant. When he was examined at the clinic a mass was noted which seemed to be about the size of a pigeon's egg and fairly movable. A roentgenogram of the colon showed multiple diverticula of the entire large bowel with a mass in the region of the cecum which seemed to be extrinsic and posterior to the bowel. Leucocytes numbered 9,500 per cubic millimeter of blood and examination of the urine gave negative results. At operation the tumor proved to be a perforated walled off diverticulum of the cecum. The pocket of the diverticulum was opened and the opening into the cecum was closed with chromic catgut and silk. The wall of the diverticulum was excised and the appendix was removed. The postoperative course was uneventful, the wound healed without drainage, and the patient was dismissed from the hospital on the twenty first day. When he returned to the clinic ten years later his only complaint was from the headaches associated with severe hypertension.

CASE 6—The patient was a woman, 45 years of age. She had suffered from several attacks of indigestion in the year before she came to the clinic. She had pain in the right lower quadrant of the abdomen, associated with constipation. Examination at the clinic had just started when she complained of pain in the right lower quadrant. Tenderness was noted over the cecum and right adnexa. Leucocytes numbered 14,700 per cubic millimeter of blood with 90 per cent polymorphonuclear leucocytes. A diagnosis of appendicitis was made and exploration was performed. When the peritoneum was opened, there was considerable exudate and muddy fluid about the cecum and pelvis. The appendix was removed. As the cecum was lifted up, there appeared several small diverticula on its

lateral and posterior surface, one of which was severely inflamed and necrotic, but did not seem to be perforated. The diverticula were not removed. Ten grams of sulfathiazole were placed over the region and the abdomen was closed without drainage. The pathologist reported chronic appendicitis with subacute periappendicitis. The postoperative course was uneventful and the patient was dismissed on the thirteenth day. She was put on a low residue diet and has had no return of the attacks, except for occasional burning sensation with bowel movements.

CASE 7—The patient was a man, 48 years of age. The most acute attack of diverticulitis had come three weeks before he visited the clinic. He had been seized with sudden, severe, colicky pain in the right side and his physician had noted a large tender mass in the right lower quadrant. The mass had partially resolved under conservative treatment with the use of mineral oil and heat. Intravenous urograms made by his physician were said to have been negative.

On examination at the clinic the patient's abdomen showed a scar in the right upper quadrant from cholecystectomy and appendectomy, which he stated had been done three years before. In the right lower quadrant was a mass the size of an orange, freely movable. It was only slightly tender. Roentgenologic examination of the colon showed multiple diverticula of the cecum associated with an extrinsic or intrinsic mass near the ileocecal valve. Leucocytes numbered 8,600 per cubic millimeter of blood.

Operation revealed a perforating lesion of the cecum which was firmly adherent to the anterior abdominal wall, forming an indurated mass measuring 4 by 5 cm. Attached to the mass were numerous loops of small bowel. Ileotransversostomy was performed. The ileum was divided about ten inches (25 cm.) from the ileocecal valve, both ends were turned in, and a side to side anastomosis was made between the proximal end of the ileum and the right half of the transverse colon. It was hoped that the mass would disappear when the fecal stream was thus by-passed. Five grams of sulfathiazole were inserted into the peritoneal cavity and the incision was closed without drainage.

The patient got along fairly well for three months but the mass persisted. He re-registered at the clinic later and right colectomy was performed. The pathologist reported that at the junction of the cecum and ascending colon there were multiple small diverticula (diverticulosis). One of these diverticula had perforated, forming a pericecal inflammatory mass 4 by 4 by 3 cm. (diverticulitis). The patient had a second uneventful postoperative course and was dismissed from the hospital on the thirteenth postoperative day.

CASE 8—The patient, a man 40 years of age, was admitted directly to the hospital complaining of a low grade ache in the right lower quadrant which had been present the previous thirty hours. He had not had any major gastrointestinal symptoms previous to that time. Five hours before admission the pain had become much more severe and was described as being colicky. Leucocytes numbered 13,700 per cubic millimeter of blood with 85 per cent polymorphonuclear leucocytes. Examination of the urine gave negative results. On physical examination the entire right side of the abdomen was found to be very tender and rigid. A diagnosis of acute appendicitis was made and operation was performed. When the peritoneum was opened through a right rectus incision, thick purulent fluid was noted in the right lower quadrant. There was also a considerable inflammatory reaction around the cecum. The appendix did not seem greatly inflamed but it was removed. When a piece of fat over the lower anterior wall of the cecum was lifted a fecalith was found to be protruding through the end of a small acutely inflamed diverticulum. The fecalith was pushed into the lumen of the bowel, the diverticulum was incised into the cecum and the opening was closed with a chromic catgut suture. A piece of fat was sutured to the cecum. The sigmoid was sutured to the cecum. Sulfathiazole was placed in the incision.

The postoperative course was uneventful, the patient being dismissed from the hospital on the thirteenth day.

TABLE I DATA ON CASES OF ACUTE DIVERTICULITIS OF THE CECUM REPORTED IN THE LITERATURE

AUTHOR	YEAR	AGE (YR.)	SEX	GROSS APPEARANCE AT OPERATION	OPERATION
Baggett ¹⁵	1941	32	M	Tumor size of Brazil nut	Il coecal resection*
Baker and Carblet ⁴	1913	34	M	Mass involving entire cecum	Cecectomy with ileotransverse colostomy*
Baker and Carblet ⁴	1943	59	M	Inflamed mass 15 cm from appendix	Excision and closure*
Barber ⁸	1938	45	F	Perforating tumor	Inverted with purse string suture*
Bearse ¹¹	1939	19	F	Mass size of tennis ball, top of cecum, full of pus	Drained, x ray view later showed single diverticulum*
Bennett Jones ¹	1937	21	F	Mass 15 cm diameter, on anterior aspect of cecum	Excision and closure in layers*
Bennett Jones ¹	1937	28	F	Mass, anterior aspect of cecum	Excision and closure in layers*
Bennett Jones ¹	1937	26	M	Mass, posterolateral surface of cecum	Right colectomy with end to side anastomosis*
Bryan ⁸	1930	28	F	Large irregular mass lateral to cecum	Cecectomy*
Bryan ⁸	1930	30	M	Numerous small inflamed masses in cecum	Right colectomy*
Burgess ³	1940	42	F	Small inflamed diverticulum	Diverticulectomy and appendectomy*
Burgess ³	1940	36	F	Lateral inflamed mass	Excision and closure*
Burgess ³	1940	60	F	Mass size of hen's egg	Excision and closure*
Burgess ³	1940	22	F	Inflamed diverticulum	Appendectomy and drainage*
Busch and Friedfeld ¹	1942	25	F	35 cm mass on lateral side of cecum	Excision and closure*
Carroll ¹²	1943	56	F	Mass 5 cm above junction of ileum and cecum	Right colectomy*
Conway and Hitzrodt ¹¹	1931	44	F	Mass size of two fists in volving cecum	Right colectomy†
Conway and Hitzrodt ¹¹	1931	32	M	Perforating diverticulum near valve with peritonitis	Diverticulectomy†
Conway and Hitzrodt ¹¹	1931	53	M	Diverticulum of lower lateral cecum	Diverticulectomy*
Cooke ¹²	1922	51	M	Not stated	Cecectomy*
Dalger and Coureaud ¹³	1927	20	M	Posterolateral perforation but the neck of the diverticulum did not connect with the lumen of the cecum	Appendectomy and diverticulectomy*
Di Argen courti ¹⁴	1944	35	F	Anterior, 76 cm diameter	Diverticulectomy and appendectomy*
Helitsla ¹³	1939	42	M	Hazelnut sized mass near appendix	Excision and closure*
Doppler ¹²	1936	1	1	Tumor anterior cecum	Ileocecal resection†
Epstein ¹⁷	1933	62	F	Mass near cecum	Excision and inversion*
Fasano ¹⁸	1937	34	M	Anterolateral tumor	Inverted diverticulum and closed*
Finfield ¹⁹	1927	1	1	Mass over cecum	Ligated and removed*
Finfield ¹⁹	1927	1	1	Mass over cecum	Ligated and removed*
Finfield ¹⁹	1927	1	1	Mass over cecum	Ligated and removed*
Fossati ¹⁰	1942	53	M	Egg sized tumor, high on lateral wall	Right colectomy*

(Table I continued on following pages)

lateral and posterior surface, one of which was severely inflamed and necrotic but did not seem to be perforated. The diverticula were not removed. Ten grams of sulfathiazole were placed over the region and the abdomen was closed without drainage. The pathologist reported that the mass was low in position and no movements.

CASE 7—The patient was a man, 45 years of age. The most acute attack of diverticulitis had come three weeks before he visited the clinic. He had been seized with sudden, severe, colicky pain in the right side and his physician had noted a large tender mass in the right lower quadrant. The mass had partially resolved under conservative treatment with the use of mineral oil and heat. Intravenous urograms made by his physician were said to have been negative.

On examination at the clinic the patient's abdomen showed a scar in the right upper quadrant from cholecystectomy and appendectomy, which he stated had been done three years before. In the right lower quadrant was a mass the size of an orange freely movable. It was only slightly tender. Roentgenologic examination of the colon showed multiple diverticula of the cecum associated with an extrinsic or intrinsic mass near the ileocecal valve. Leucocytes numbered 8,600 per cubic millimeter of blood.

Operation revealed a perforating lesion of the cecum which was firmly adherent to the anterior abdominal wall, forming an indurated mass measuring 4 by 5 cm. Attached to the mass were numerous loops of small bowel. Ileotransversostomy was performed. The ileum was divided about ten inches (25 cm) from the ileocecal valve. Both ends were turned in, and a side to side anastomosis was made between the proximal end of the ileum and the right half of the transverse colon. It was hoped that the mass would disappear when the fecal stream was thus bypassed. Five grams of sulfathiazole were inserted into the peritoneal cavity and the incision was closed without drainage.

The patient got along fairly well for three months but the mass persisted. He re-registered at the clinic later and right colectomy was performed. The pathologist reported that at the junction of the cecum and ascending colon there were multiple small diverticula (diverticulosis). One of these diverticula had perforated forming a pericecal inflammatory mass 4 by 4 by 3 cm (diverticulitis). The patient had a second uneventful postoperative course and was dismissed from the hospital on the thirteenth postoperative day.

CASE 8—The patient a man 40 years of age was admitted directly to the hospital complaining of a low grade ache in the right lower quadrant which had been present the previous thirty hours. He had not had any major gastrointestinal symptoms previous to that time. Five hours before admission the pain had become much more severe and was described as being colicky. Leucocytes numbered 13,700 per cubic millimeter of blood with 85 per cent polymorphonuclear leucocytes. Examination of the urine gave negative results. On physical examination the entire right side of the abdomen was found to be very tender and rigid. A diagnosis of acute appendicitis was made and operation was performed. When the peritoneum was opened through a right rectus incision thick purulent fluid was noted in the right lower quadrant. There was also a considerable inflammatory reaction around the cecum. The appendix did not seem greatly inflamed but it was removed. When a piece of fat over the lower anterior wall of the cecum was lifted a fecalith was found to be protruding through the end of a small acutely inflamed diverticulum. The fecalith was pushed into the lumen of the bowel the diverticulum was inverted into the cecum and the opening was closed with a chromic catgut suture. A piece of fat was sutured over this. Exploration of the colon did not reveal any other diverticula. The sigmoid was palpated for the presence of diverticula but none were felt. Ten grams of sulfathiazole were inserted intraperitoneally and 5 Gm of sulfanilamide were placed in the incision.

The postoperative course was uneventful the patient being dismissed from the hospital on the thirteenth day.

TABLE I DATA ON CASES OF ACUTE DIVERTICULITIS OF THE CECUM REPORTED IN THE LITERATURE

AUTHOR	YEAR	AGE (Y.R.)	SEX	GROSS APPEARANCE AT OPERATION	OPERATION
Baggett ¹	1941	32	M	Tumor size of Brazil nut	Ileocecal resection*
Baker and Carlile ⁴	1943	34	M	Mass involving entire cecum	Cecectomy with ileotransverse colostomy*
Baker and Carlile ⁴	1943	59	M	Inflamed mass 15 cm from appendix	Excision and closure*
Barbier ⁶	1933	45	F	Perforating tumor	Inverted with purse string suture*
Bearse ⁷	1939	19	F	Mass size of tennis ball, top of cecum, full of pus	Drained, x ray view later showed single diverticulum*
Bennett Jones ¹	1937	21	F	Mass 15 cm diameter, anterior aspect of cecum	Excision and closure in layers*
Bennett Jones ²	1937	28	F	Mass, anterior aspect of cecum	Excision and closure in layers*
Bennett Jones ²	1937	26	M	Mass, posterior aspect of cecum	
Bryan ³	1930	29	F	Large irregular to cecum	
Bryan ³	1930	30	M	Numerous small inflamed	Right colectomy*
Burgess ⁵	1940	42	F		age*
Burgess ⁵	1940	30	F		
Burgess ⁵	1940	60	F		
Burgess ⁵	1940	22	F		
Busch and Friedfeld ³	1942	25	F	25 cm mass on lateral side of cecum	Excision and closure*
Carroll ¹⁰	1943	56	F	Mass 5 cm above junction of ileum and cecum	Right colectomy*
Conway and Hitzrot ¹¹	1931	44	F	Mass size of two fists in	Right colectomy†
Conway and Hitzrot ¹¹	1931	32	M		
Conway and Hitzrot ¹¹	1931	53	M		
Cooke ¹²	1922	51	M	erat cecum Not stated	Cecectomy*
Dalger and Courcaudis	1927	20	M	Posterolateral perforation but the neck of the diverticulum did not connect with the lumen of the cecum	Appendectomy and diverticulectomy*
D'Argencourt ¹⁴	1944	35	F	Anterior, 76 cm diameter	Diverticulectomy and appendectomy*
Delitala ¹⁵	1939	42	M	Hazelnut sized mass near appendix	Excision and closure*
Doppler ¹⁶	1936	†	†	Tumor anterior cecum	Ileocecal resection†
Epstein ¹⁷	1933	62	F	Mass near cecum	Excision and inversion*
Fasano ¹⁸	1937	34	M	Anterolateral tumor	Inverted diverticulum and closed*
Fineldis	1927	†	†	Mass over cecum	Ligated and removed*
Fineldis	1927	†	†	Mass over cecum	Ligated and removed*
Fineldis	1927	†	†	Mass over cecum	Ligated and removed*
Fossatizo	1942	53	M	Egg sized tumor high on lateral wall	Right colectomy*

(Table I continued on following pages)

TABLE I—Cont'd

AUTHOR	YEAR	AGE (YR.)	SEX	GROSS APPEARANCE AT OPERATION	OPERATION
Freeman ²¹	1927	40	M	Congested diverticulum just above valve	Diverticulectomy*
Frehling ²²	1933	51	F	Smooth lateral mass	
Frehling ²³	1945				
French ²⁴	1923				
French ²⁴	1923				
Fritz ²⁵	1943				
Gant ²⁶	1921				
Gatewood ²⁷	1943				
Gatewood ²	1945				
				of hen's egg	pendectomy*
Grace ²⁸	1940	37	F	Anterior mass, size of egg yolk	Diverticulectomy*
Grace ²⁸	1938	40	M	Posterior mass, size of egg yolk	Right colectomy*
Graves ³⁰	1938	f	F	Lateral mass 2 cm. diameter	Exteriorized and removed in ten days*
Graves ³⁰	1938	f	M	6 cm. mass lateral with subacute perforation	Drained, postoperative fistula for one year*
Greensfelder and Miller ³¹	1929	38	F	Traction diverticulum at base	Freed and inverted†*
Greensfelder and Miller ³¹	1929	46	M	Lateral mass, size 1 by 2 cm.	Diverticulectomy*
Hendlin ³²	1944	17	F	Feces free in abdomen from 13 cm. perforation of diverticulum	Diverticulectomy and appendectomy*

				cm	
Klages ³⁶	1937	52	M	2 cm. tumor above appendix	Excised tumor and appendix*
Leonardo ³⁷	1930	63	F	Superior mass 5 by 3.8 cm.	Diverticulectomy and appendectomy*
McBee ³⁸	1940	42	F	Inflamed mass medial side	Right colectomy*
McBee ³⁸	1940	32	F	Mass size of egg	Right colectomy*
McVay ³⁹	1927	36	M	Medial mass 2 by 1.5 cm	Diverticulectomy and appendectomy*
McWhorter ⁴⁰	1934	19	M	Perforating mass, antero lateral	Closure of neck of diverticulum*
McWhorter ⁴⁰	1934	34	M	Lateral mass 1.5 cm diam etc	Excision*
Mosehowitz ⁴¹	1918	44	M	Inflamed epiploic tag containing diverticulum	Removal and closure*
Odenour ⁴²	1939	52	M	Gangrenous mass at junction	Diverticulectomy and appendectomy*
O'Callaghan ⁴³	1937	68	F	Tumor size of child's head	Diverticulectomy*
Owings and Moran ⁴⁴	1940	42	F	Lateral mass as large as hand	Right colectomy*

TABLE I—CONT'D

AUTHOR	YEAR	AGE (YR.)	SEX	GROSS APPEARANCE AT OPERATION	OPERATION
Pereira ⁴⁵	1927	54	M	13 cm diverticulum near appendix	Cecectomy*
Pessagno ⁴⁶	1913	52	F	Medial border size of hen's egg	Cecectomy*
Porter ⁴⁷	1913	60	F	Lateral mass 2 cm diameter	Right colectomy†
Potter ⁴⁸	1912	32	F	"	Diverticulectomy and appendectomy*
Rogers and Hilton ⁴⁹	1930	39	M	Medial mass 2 cm diameter	Partial cecectomy*
Sammartino and Cervini ⁵⁰	1939	66	F	Walled off abscess behind cecum and generalized peritonitis	Diverticulectomy and appendectomy*
Schnug ⁵¹	1943	30	M	25 by 25 cm mass 3 cm above valve	Diverticulectomy*
Schnug ⁵¹	1943	59	M	Whole cecum in a mass (inflamed)	Right colectomy*
Schnug ⁵¹	1943	31	M	"	Diverticulectomy*
Schnug ⁵¹	1943	29	M	"	Diverticulectomy and appendectomy*
Schnug ⁵¹	1943	66	F	Pericecal abscess	Drain†
Schnug ⁵¹	1943	47	M	Acute inflamed diverticulum	Appendectomy and diverticulectomy*
Shumizu ⁵²	1937	49	M	3 cm mass near valve	Excised*
Staley ⁵³	1939	56	F	4 cm mass 1 cm from appendix	Diverticulectomy*
Stetten ⁵⁴	1936	35	F	2 cm above valve mass size of thumb	Right colectomy*
Stewart ⁵⁵	1930	54	M	Diverticulum 1 by 15 cm	Right colectomy†
Sumi ⁵⁶	1936	57	M	Walnut sized mass 1 cm from valve	Ileocecal resection*
Szabo ⁵⁷	1934	29	F	Nut sized mass anterior cecum	Cecal resection*
Gordon Taylor ⁵⁸	1939	60	M	Lemon sized mass near valve	Right colectomy†
Thomsen ⁵⁹	1930	55	M	Large diverticulum with torsion	Excision*
Thomsen ⁵⁹	1935	54	F	Walnut sized lateral mass	Right colectomy*
Thomsen ⁵⁹	1935	23	M	25 cm diameter mass lateral	"*
Tschudi ⁶⁰	1936	54	M	Walnut sized tumor near valve	Cecectomy†
Walking ⁶¹	1941	43	M	Mass of inflamed tissue with abscess opening in cecum	Drained abscess†
Weible ⁶²	1937	54	F	Apple sized mass anterior	Cecectomy*
Weible ⁶²	1937	30	M	Anterior mass	Closed with purse string suture*
Wilson ⁶³	1932	1	F	Inflamed diverticulum of cecum	Diverticulectomy*

*Patient recovered

†Patient died

‡Result not stated

§Patient died from gangrene of the intestine

ANALYSIS OF DATA

Some data on the ninety one cases in the literature are shown in Table I. Combining information from these with the eight cases in the clinic records brings out some rather interesting results

TABLE I—CONT'D

AUTHOR	YEAR	AGE (YR.)	SEX	GROSS APPEARANCE AT OPERATION	OPERATION
Freeman ²¹	1927	40	M	Congested diverticulum just above valve	Diverticulectomy*
Frehling ²²	1931	51	F	Smooth lateral mass	Sigmoid colectomy*
Frehling ²³	1945	37	M	Mass posterior wall of cecum	Exteriorized, draining sinus developed*
Gatwood ¹⁷	1915	21	M	Retropetitoneal mass, size of hen's egg	Diverticulectomy and appendectomy*
Grace ²⁴	1940	37	F	Anterior mass, size of egg yolk	Diverticulectomy*
Grace ²⁵	1939	40	M	Posterior mass, size of egg yolk	Right colectomy*
Graves ¹⁰	1939	1	F	Lateral mass 2 cm. diameter	Exteriorized and removed in ten days*
				— as it contained a sub-ileal diverticulum	Drained, postoperative fistula for one year*
				at ileal and inserted*	
Green*Feller and Miller ²⁶	1929	46	M	Lateral mass, size 1 by 2 cm	Diverticulectomy*
Hendtlass ²⁷	1944	17	F	Feces free in abdomen from 1.3 cm perforation of diverticulum	Diverticulectomy and appendectomy*
Jackson ²⁸	1917	23	F	Lateral mass 6.4 by 7.6 cm	Cecectomy†
Jonas ²⁴	1940	50	F	?	Excision and inversion*
Jonas ²⁴	1940	29	F	?	Cecectomy*
Jonas ²⁴	1940	47	M	?	Excision and inversion*
Jonas ²⁴	1940	49	F	?	Excision and inversion*
Jonas ²⁴	1940	36	F	?	Excision and inversion*
Kennon ²⁹	1933	26	M	Posterior mass 6.3 by 1.3 cm	?
Klages ³⁰	1937	52	M	2 cm. tumor above appendix	Excised tumor and appendix*
Leonardo ²⁷	1930	63	F	Superior mass 5 by 3.8 cm.	Diverticulectomy and appendectomy†
McBee ³⁵	1940	42	F	Inflamed mass medial side	Right colectomy*
McBee ³⁵	1940	32	F	Mass size of egg	Right colectomy*
McNay ³⁰	1927	36	M	Medial mass 2 by 1.5 cm	Diverticulectomy and appendectomy*
McWhorter ³⁰	1934	19	M	Perforating mass antero lateral	Closure of neck of diverticulum*
McWhorter ³⁰	1934	34	M	Lateral mass 1.5 cm. diameter	Excision*
Moschowitz ⁴¹	1918	44	M	Inflamed epiploic tag containing diverticulum	Removal and closure*
Obenour ³²	1938	52	M	Gangrenous mass at junction	Diverticulectomy and appendectomy*
O Callaghan ⁴²	1937	69	F	Tumor size of child's head	Diverticulectomy*
Owings and Morgan ⁴⁴	1940	42	F	Lateral mass as large as hand	Right colectomy*

SUMMARY

Although diverticula of the cecum are considered rather rare, we were able to find records of ninety nine cases in which operation had been performed because of acute diverticulitis of the cecum. The average age incidence of the patients was less than forty years, making it much lower than for diverticulitis in the remainder of the colon. The cases were about equally distributed between the two sexes, an observation which is also different from most studies on surgical diverticulitis, which show a preponderance of males. More than one third of the surgeons performed extensive operations such as resection of the cecum or right colectomy. This is understandable in view of the difficulty of distinguishing a perforated and inflamed diverticulum from carcinoma at operation. Eighty-four per cent of the surgeons listing a preoperative diagnosis thought the appendix to be the cause of the patient's symptoms previous to operation.

We believe that acute diverticulitis of the cecum is a surgical disease and will continue to be so for a long time to come, since it seems very difficult to distinguish from appendicitis preoperatively, and since roentgenologic studies of the colon following barium enemas obviously are usually contraindicated when the most probable diagnosis in a case is appendicitis.

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Age—The average age of all the patients who underwent operation was 39.1 years. The women averaged 41.6 years of age, the men 36.6. This is striking in view of the fact that surgical diverticulitis is usually considered to be a disease which attacks persons past middle age.

Sex—The sex of the patients was given in ninety-two of the ninety-nine cases. Forty-five were women and forty-seven men. This too is unusual since practically all studies of patients on whom operation for diverticulitis has been performed show a heavy preponderance of males.

Operative Mortality Rate—Of the ninety-four cases in which the outcome of operations was reported, in six it was stated that the patient failed to recover, thus giving an over-all mortality rate of 6.4 per cent. This is considerably lower than the mortality rate in most published series of cases of surgical diverticulitis. In two of the six cases in which the patients died, right colectomy was performed; in one, cecectomy; in two, simple excision of the diverticulum, and in one the diverticulum was merely drained.

Choice of Operation—In ninety-six cases the authors stated their choice of operation.

Fifty-three surgeons performed simple excision or diverticulectomy. Two patients died, a mortality rate of 4 per cent.

One surgeon simply put sulfathiazole in the abdomen and left the diverticulum alone.

Eighteen surgeons performed right colectomy. Two patients died, a mortality rate of 11 per cent.

Three surgeons performed simple closure of the defect.

Fourteen surgeons performed cecectomy, anastomosing the terminal ileum to the ascending colon. One patient died, a mortality rate of 7.1 per cent.

Five surgeons used simple drainage. One patient died, a mortality rate of 20 per cent.

Two surgeons exteriorized the mass in a Mikulicz type of procedure. Neither of the patients died.

Preoperative Diagnosis—The preoperative diagnosis was stated in sixty-three of the cases. In forty-three it was acute appendicitis; in six, appendiceal abscess; in two, perforated appendix; in two, ruptured appendix; in two, degenerating fibroids; in two, salpingitis; in two, carcinoma; and in four, diverticulitis. Thus 84 per cent of the stated preoperative diagnoses were of some type of appendicitis. In only 6 per cent of the cases was the condition diagnosed preoperatively before operation as diverticulitis.

Operative Diagnosis—A major operation was done in a high percentage of the cases: right colectomy in eighteen cases and resection of the cecum in

We believe a study of the
this. The reason lies in the
inflammatory mass of a per-
forating diverticulum and a perforating carcinoma. Since carcinoma is much
more common in the cecum than a diverticulum, a radical approach was adopted.
Experience will probably not change this situation, since right colectomy was
performed for acute diverticulitis of the cecum by some of the most experienced
surgeons reporting in the series.

SUBCUTANEOUS HEPARIN IN THE TREATMENT OF ARTERIAL THROMBOTIC DISEASE

PRELIMINARY REPORT

I H RICHTER MD H B EDLER MD, AND LEO LOEWEL, MD
BROOKLYN, N Y

(From the Thromboembolic Disease Unit and the Peripheral Vascular Disease Clinic of the Jewish Hospital of Brooklyn)

THE results in the conservative treatment of venous thromboembolic disease with subcutaneous heparin in the Pitkin menstruum^{*} have been so gratifying it seemed logical to apply this therapy in the management of arterial thrombotic disease. Exploratory studies were done in fifteen patients in order to observe the clinical deportment of this preparation in the presence of various types of intra arterial clotting. The clinical observations were so promising that a preliminary report seems justified.

TREATMENT PROGRAM

Heparin/Pitkin menstruum^{*} is a preparation of various amounts of heparin sodium salt, with or without vasoconstrictor drugs, dissolved in the Pitkin menstruum. The dosage of heparin may be varied as indicated in the treatment of the individual patient. In general the anticoagulant action of heparin sodium salt combined with vasoconstrictor drugs (in the menstruum) is more prolonged than the same amount of heparin sodium salt (in the menstruum) without vasoconstrictor drugs. In thromboembolic venous disease heparin with vasoconstrictor drugs is customarily employed. It is advisable, however, to use heparin without vasoconstrictor drugs in thrombotic arterial disease in order to obviate the complicating factor of arterial spasm. This may necessitate more frequent administration because of the more rapid depletion of the individual deposit.

Body weight and individual reactivity dictate the amount of heparin/Pitkin menstruum to be used in a given case. For the initial injection body weight is employed as a guide. Patients weighing up to approximately 200 pounds (90.0 kg.) should be given an initial dose of 400 mg. of heparin sodium salt. Subsequently the dosage should be adjusted according to the intensity of the "heparin effect" as estimated by the coagulation time. Compared with a normal coagulation time of nine to fifteen minutes (Lee White modification of Howell's method), a coagulation time of thirty to sixty minutes is considered an adequate "heparin effect". In the average case 400 mg. of heparin should be sufficient to keep the patient heparinized for approximately two days

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Thereafter, 400 mg should be administered every second day throughout the requisite period of heparinization. If the patient receives a blood transfusion during this treatment period, 400 mg should be administered immediately following the transfusion, irrespective of when or how many previous deposits have been given. If, for any reason, there is need to stop the effect of the heparinization this can be accomplished immediately by the intravenous administration of 250 to 500 cc of whole blood or bank blood not more than three days old.

THE METHOD OF ADMINISTRATION

- 1 Warm the ampule gently either by holding it under running hot tap water or immersing in a container of hot tap water until the contents become fluid.
- 2 Draw the contents of the ampule into a dry, sterile 5 or 10 cc syringe, using a sterile needle 18 gauge (two inch length). After the contents have been drawn up the 18 gauge needle may be replaced by a 20 gauge needle for the actual injection.
- 3 Inject the contents immediately into the deep subcutaneous (or superficial intramuscular) tissue, preferably in the anterior or lateral aspect of the thigh. When subsequent injections are required use the right and left thighs alternately and avoid sites of previous injection. Do not inject into sites where pressure may be exerted upon the injection area.
- 4 Be certain that the contents of the syringe are not too hot prior to the injection. The syringe and contents should feel only slightly warm.
- 5 Do not apply either cold or heat to the area of deposition unless for purpose of retarding or accelerating release of the drug.

THE METHOD OF FOLLOWING THE PATIENT'S CLINICAL COURSE

The effect of heparin is judged by and based upon determination of the blood coagulation time which should be estimated daily throughout the period of heparinization. The capillary tube method is inaccurate and should not be used. The Lee White modification of Howell's method for determination of blood coagulation time is as follows:

- 1 Place four chemically clean dry 7.5 by 10 mm test tubes in a rack.
- 2 With a sterile dry syringe and needle, withdraw a little more than 1.5 cc of venous blood from the subject. The test is timed from the moment the blood is first observed in the syringe. Remove the needle from the syringe.
- 3 Gently distribute a little more than 0.5 cc of blood into each test tube. Disrupt the last air-containing fraction.
- 4 All glassware, syringes and needles must be absolutely dry. Moisture, alcohol, etc. invalidate the determination.
- 5 The vein must be negotiated cleanly. If difficulty is encountered it is better to use a fresh needle and syringe. Even a small amount of tissue juice aspirated into the syringe will give a false result.
- 6 Once the blood is placed in the test tubes they must be disturbed as little as possible while observing for the end point. It will be noticed that well heparinized blood will sediment very rapidly. The tubes should not be shaken after sedimentation of the blood. Look for clotting in the red cell layer as well as in the plasma layer by gently tilting the tubes. In unclotted blood the red cell layer will flow as the tube is angled.
- 7 First gently tilt one tube and note the flow of the red cell layer. If the flow is rapid, discard the tube and wait about five minutes before the second tube is angled. In this way the end point may be approximated and then finally accurately determined from the third or fourth tubes. Once any of the tubes is disturbed it should be discarded.
- 8 The patient's coagulation time should be determined before heparinization for control purposes. After that the coagulation time should be estimated daily (twenty-four hours after the heparin injection and immediately before the next heparin injection).

Papaverine is used concomitantly in liberal dosages first by the intramuscular or intravenous route in 1 to 3 gr dosages and subsequently by mouth in maintenance dosages of 1 to 1½ gr every four hours. Paravertebral sympathetic blocks are used when indicated and repeated whenever necessary in the presence of protracted vasospasm. The vasospasm is apparent for the most part during the early stages of the treatment program before heparinization is in full effect. Rarely is sympathetic block necessary following the first or second deposit of heparin/Pitkin menstruum. Additional treatment measures include antibiotics parenterally and topically to combat infection, symptomatic therapy, adequate sedation, and control of diabetes when present.

TECHNIQUES OF FOLLOWING AND EVALUATING THE PROGRESS OF THE PATIENT

Thermocouple, oscillographic, and histamine skin tests were performed routinely on all of the patients before heparinization was initiated. These studies were carried out repeatedly thereafter in order to assess the response to the treatment program.

The clinical criteria of improvement were (1) the restoration to the compromised tissues of normal color, tone, and turgor; (2) delineation of any gangrenous process; (3) decrease in pain; (4) increase in pulsations of blood vessels of the affected limb. The clinical improvement was usually reflected in the oscillographic studies, surface temperature readings, and histamine skin reactions.

CLINICAL MATERIAL

The effectiveness of heparin in the Pitkin menstruum was investigated in this series of cases merely as an exploratory study. The patients represented many aspects of arterial thrombotic disease and served adequately as a means of appraising the clinical response to this preparation. The various arterial lesions included in this series of 15 patients (Table I) were intra-arterial emboli (5 cases), diabetic gangrene (6 cases), thromboangitis obliterans (3 cases), and ergotism (1 case).

DISCUSSION OF RESULTS

Although the pathogenesis differs in the various diseases enumerated in Table I, the common denominator is thrombus formation. While recanalization of thrombus may supervene sufficiently to maintain the vascular stream and retain the viability of the affected limb, as a rule death of tissue and gangrene is the ultimate fate in the untreated case of intra-arterial thrombotic occlusion. Through the use of anticoagulants such as heparin, propagation of thrombus is inhibited, the patency of the affected vessel and uninvolved collaterals is maintained. As a result, loss of tissue is minimized or completely obviated and recanalization of the affected major vessel is enhanced.

Of the five patients with intra-arterial embolization, the result was successful in four and there was one treatment failure. A favorable outcome in all of the four patients was indicated by disappearance of cyanosis, prompt amelioration of pain indicating restoration of circulation, and more important, the absence of necrosis. The clinical improvement was documented by elevation

TABLE I HEPARIN/PITEN MENSTRUUM IN THE TREATMENT OF FIFTEEN PATIENTS WITH ARTERIAL THROMBOTIC DISEASE

CASE NO	SEX	AGE	DIAGNOSIS	DURATION	CLINICAL FINDINGS PRIOR TO THERAPY	DAYS	HUAREN TREATMENT	RESULTS AND REMARKS	
1	D	P	M	50	Embolus left femoral artery arterio-sclerotic heart disease, auricular fibrillation	13 hr	12	2,100	Embolus restored, occlusive readings at knee 0.5, ankle 0.5, skin temperature, first toe 74.5° F, histamine skin test, foot, normal
2	S	F	T	60	1 Embolus right femoral artery, arterio-sclerotic heart disease 2 Embolus right brachial artery	8 hr	5	1,050	Color normal, occlusive readings at knee and thigh, skin temperature and histamine skin test perceptibly improved
3	R	J	M	49	Embolus right popliteal artery	20 hr	9	1,750	Color normal, no necrosis
4	H	P	M	70	Embolus right popliteal artery coronary artery thrombosis	7 wk	9	1,750	Dorsalis pedis and posterior tibial pulsations present, color and tissue tone normal, pain disappeared, skin temperature normal
5	R	W	M	78	Saddle embolus of aorta pulmonary embolus	14 hr	5	600	Gangrenous process arrested, amputation performed because of intractable pain
6	S	K	F	72	Bilateral gangrene	7 days	14	2,500	Normal color restored, occlusive readings right knee, 0.5, right ankle, 0, left knee, 0.5, left ankle, 0
7	L	S	F	56	Bilateral gangrene	4 1/2	-	2,450	Gangrenous process controlled until patient refused further treatment, toe finally amputated
8	A	H	F	60	Bilateral gangrene	2 wk	1-	1,100	Gangrene extended requiring amputation

1- Gangrene finally controlled and debrided, patient anxious to amputate, toes sloughing off, histamine skin test, right thigh 0.5, right ankle 0.5, left thigh 0.5, left ankle 0.5, skin temperature, first toe 74.5° F, histamine skin test, foot, normal

9	M R T	53	Diabetic gangrene	- no dry 2 days wet	Gangrene of left big toe with cellulitis of foot and adjoining two toes despite penicillin dosages, pelis and posterior tibial absent, oscilometric readings thigh 0.5, knee flicker, ankle, flicker	2 150	Cellulitis disappeared, gangrene delinked with sloughing off of toe, oscilometric readings, thigh, 1.0, knee, 0.5, ankle, flicker
10	M K M	61	Diabetic gangrene	4 wk	Gangrene left third toe and ulbon ing 1 1/2 inches of foot, cellulitis with half of second toe and a long half of foot which spread despite sulfonamides and penicillin, pallor of foot on elevation	2 500	Gangrene demarcated, cellulitis subsided, toe sloughing off
11	M N F	73	Diabetic gangrene	1 wk	Extensive gangrene of medial surface of left big toe and entire third and fifth toes and adjoining part of foot necrotic blister on heel com plecting infection with fetid odor, penicillin alone ineffectual, oscilometric readings knee, 1, ankle flicker, amputation indicated but patient refused to consent	2 650	Gangrene delinked with sloughing off of third toe, infection controlled with residual open wound on plantar surface, skin around ulcer healthy, oscilometric readings, knee, 2.0, ankle 0.75
12	M N M	38	Thromboangitis obliterans	90 days	Extensive gangrene of right ankle and foot with severe secondary infection oscilometric readings knee flicker, ankle, 0	2 150	Conjoint heparin and penicillin treatment interrupted because of lack of cooperation of patient, gangrene extended resulting in amputation
13	J C M	42	Thromboangitis obliterans	30 days	Left radial pulse absent, left hand especially dorsum, painful, blanched with cyanosis at periphery, hand cold with loss of tissue tone	2 650	Left radial pulse restored with disappearance of blanching, surrounding cyanosis, coolness and pain, improvement so singular patient enabled to return to work as bartender
14	C C M	42	Thromboangitis obliterans, thrombophlebitis migrans	5 wk	Extensive thrombophlebitis of left leg with swelling, pain, and positive Homans' sign, diminished arterial pulsations with history of intermittent claudication, reduced to absent oscilometric readings of left lower extremity	2 400	Rapid resolution of thrombophlebitis with disappearance of pain, swelling and tender ness increase in arterial pulsations
15	B G F	60	Frogman	18 hr	Bilateral intense, cold cyanosis of hands with absent radials, no response to sympathetic block, oscilometric readings at wrists absent, skin temperature, right thumb, 82.5° F left thumb 78° F	750	Both radial pulsations present and normal, color healthy, oscilometric readings both wrists, 1.0, skin temperature, right thumb, 85° F, left thumb 88° F

We wish to express our thanks to Dr. P. W. Ascher for referring some of the cases in this series

*The Boullite oscilometer was used Normal readings are wrists 1 to 3 thumbs 4 to 8 knees 4 to 8 ankles 2 to 3

Dr. M. A. Rabinovitz Dr. J. Rosenthal and

of surface temperature increased oscillometric readings and intensification of the histamine skin reaction. It is noteworthy that heparin/Pitkin menstruum therapy was initiated in the four successfully treated patients within eight to twenty hours after onset. The one failure (Case 4) was admitted for treatment three weeks after the embolic arterial occlusion. Failure to respond was therefore not unexpected in view of the fact that one to two days after embolic occlusion the functional pathology no longer consists merely of stagnation of blood with some complicating perivascular extravasation. Thereafter the stagnant blood becomes fibrinous and undergoes progressive organization with irreversible tissue changes. It is at this stage that anticoagulant therapy is futile. Fortunately embolic occlusion is usually accompanied by marked vasospasm; the resultant pain is so severe and excruciating and difficult to endure that patients enlist medical aid at an early stage when the treatment program might be expected to be more effective.

Of the six patients with diabetic gangrene five had a favorable result and one suffered an amputation. In this type of patient the results understandably are not as dramatic as in the embolic group because the thrombosis develops insidiously, progresses at a slower tempo and is usually unaccompanied by severe pain of the type that demands prompt relief. These patients therefore are observed at a later stage when some necrosis and gangrene have actually developed. If untreated the thrombosis is progressive and more tissue is inevitably involved with resultant loss of limb. Thus with diabetic gangrene the chief objective is to prevent further intravascular clotting, thereby salvaging as much tissue and limb as possible.

In the five patients with satisfactory outcome heparin/Pitkin therapy was instituted from three to sixty days after the onset of the gangrene. Significantly in these five patients where only mottling cyanosis was present indicating an early stage of thrombosis these affected areas improved in color under treatment and the skin temperatures rose to a higher level. Those areas already the seat of dry gangrene obviously had to be sacrificed. It is interesting to note that one patient (Case 10) was given extensive treatment for four weeks at home with both penicillin and sulfonamides despite which the lesion progressed and necrosis occurred. Following admission to the hospital penicillin was continued but it was not until after two subcutaneous deposits of heparin in the Pitkin menstruum that the necrotic lesion showed a definite area of demarcation following which the erythematous and cellulitis-like lesion receded and the bullae cleared up. Finally the erythema and bullae were no longer evident and the gangrenous area was debrided to the third toe and part of the plantar surface of the foot. In the one treatment failure (Case 7) the first, second and third toes were mummified when therapy was begun about four months after the initial appearance of gangrene.

Of the three patients with thromboangitis obliterans two responded successfully with restoration of patency of the affected and vascular channels, resumption of circulation in the affected limb and amelioration of pain and claudication. The disappearance of blanching in the digital distribution during the

therapy (Case 13) was so striking that it was difficult to distinguish between the affected and contralateral limb. The one treatment failure (Case 12) eventuated in amputation. This patient had involvement of the toes and foot up to the ankles which started three months prior to admission. He was very toxic and had a high swinging temperature. Because of lack of cooperation the conjoint program of heparin and penicillin was suspended following which the gangrene rapidly spread and extended. Amputation was ultimately carried out in another institution.

One patient had early gangrene of both hands due to ergotamine tartrate which was administered for pruritus due to jaundice. After several injections of the drug the patient developed severe cyanosis and coldness of both hands. On examination both radial pulses were absent, the skin temperature was subnormal, and the histamine skin test was negative. Both stellate ganglia were blocked without appreciable results. Subcutaneous heparin/Pitlin menstruum was started about eighteen hours after onset and prompt improvement was manifest after two deposits. Two weeks later the radial pulses were palpable and of good volume, normal color was restored, and the skin temperature, ocillometric readings, and histamine skin tests were all within normal limits.

SUMMARY AND CONCLUSIONS

Heparin Pitlin menstruum has proved to be an effective agent in the treatment of arterial thrombotic lesions. Clinical observations in fifteen cases of intra-arterial thromboses have shown satisfactory response in terms of amelioration of pain, restoration of normal color, tone and lividity to the tissues, delineation of any gangrenous process, and increase in pulsation of blood vessels in the affected parts. While this series of patients is too small to lend itself to any statistical review, the results are sufficiently encouraging to justify further expansion of this exploratory project. In general, those patients fared best who received the optimum treatment program within a few hours after the occlusive process became evident.

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THIOURACIL AND CARCINOMA OF THE THYROID

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THII; marked proliferation produced in the thyroid by thiouracil has aroused in the minds of many the question of possible subsequent development of malignancies in the patients so treated. This marked proliferation along with the high incidence of carcinoma in toxic nodular goiter has led Hinton and Lord¹ to state that thiouracil is contraindicated in the treatment of toxic nodular goiter. Pertinent also is the experimental work of Bielschowsky² who noted that rats fed thiourea and 2 acetaminofluorene developed adenomatous or anaplastic invasive tumors of the thyroid while either drug given alone did not produce such changes.

We have recently encountered a carcinoma in a patient with diffuse toxic hyperplasia of the thyroid who was treated preoperatively with thiouracil and iodine. Because of the possible carcinogenic activity of thiourea this case is reported here.

CASE REPORT

History—Mrs. W. H. D., a 56-year-old white woman was first seen on Aug. 31, 1945 complaining of nervousness, anorexia and a loss of forty nine pounds in weight during the previous year. She had also noted increasing bulging of the eyes with impairment of vision. She had noted no increase in cold tolerance or heat intolerance. There were no gastrointestinal symptoms. The past history was entirely negative.

Physical Examination—Temperature was 98.6° F., pulse 108 to 120, respirations were 20, blood pressure 158/90. Body weight was 115 pounds. The general appearance of the patient was that of an emaciated, nervous white woman with marked exophthalmos and appearing to be about the stated age. The ears, nose, and mouth were negative. The eyes showed marked exophthalmos with poor vision partially corrected by glasses. The neck showed a slight smooth fullness in the region of the thyroid, there was no bruit. The lungs were clear. The heart rhythm was regular but rapid and the sounds were of good quality. There were no murmurs. The pulse was forceful with a pulse rate varying at different times, from 108 to 120. The abdomen and extremities were negative. The only positive finding on neuromuscular examination was a constant fine tremor of both hands which was exaggerated on extension of the arms and separation of the fingers.

Laboratory—Basal metabolic rate was + 36, hemoglobin 13.6 Gm. red blood cells 4,100,000, white blood cells 7,200, with a normal differential count. The urine was negative.

Treatment and Progress (see Table I)—Treatment was begun on Aug. 31, 1945, with 1 tablet four times a day for one week. On September 7 the basal metabolic rate was + 1 with 64 per cent neutrocytes. Thiouracil was continued.

On September 14 the basal metabolic rate was + 7.900 with 60 per cent neutrocytes. At this time the weight was 116½ pounds and was then increased to 124 Gm. daily and continued for six days. On September 20 the basal metabolic rate was + 17, body weight 120 pounds, pulse 98, and the white blood cells 7,100 with 62 per cent neutrocytes.

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TABLE I PREOPERATIVE THERAPY

DATE	IPLG THERAPY DAILY DOSE		TOTAL THYORACIL (GM)	BMR	BODY WEIGHT	PULSE	WBC
	THYORACIL (GM)	LICORIN (GTT)					
5/31/45				+36	115	108-120	7,200
6/31 to 9/7	0.2		14	+21		94	9,000
9/7 to 9/14	0.3		21	+20	116½	92	7,900
9/14 to 9/20	0.4		28	+17	120	88	7,100
9/20 to 9/27	0.4		35	+19	121	72	8,100
9/27 to 10/4	0.2	20	14	+ -	120½	72	7,500
10/4 to 10/10	None	20	0.6				
			101				

Thyroracil was continued at 0.4 Gm daily until September 27 when the basal metabolic rate was +9, body weight 121 pounds, pulse 72, and the white blood cells 8,100 with 38 per cent neutrocytes. On this date thyroracil was reduced to 0.2 Gm daily and in addition 10 Gtt of Lugol's solution was given twice daily. On October 4 the basal metabolic rate was +2, body weight 126½ pounds, and the pulse 72. The white blood cell was 7,500 and the neutrocytes 60 per cent. Thyroracil was discontinued but the Lugol's solution was continued in doses of 10 Gtt twice daily up to the time of operation on October 10.

On October 10 a partial resection of both lobes of the thyroid was done. Postoperative recovery was uneventful. Because of the pathologic findings she was treated with x-ray to the thyroid region receiving 3,500 r through two portals between October 19 and November 8 at a rate of 200 r each day. Each portal measuring 8 by 8 cm. was treated on alternate days. To date, five months after surgery, there has been no clinical evidence of recurrent tumor and the patient is symptom free.

Pathology—

Gross (S45 2140). The specimen consisted of two pieces of thyroid tissue having a combined weight of 175 Gm. Externally they were pale brown, normally lobulated, and partially covered by a transparent capsule. On section they were firm, normally lobulated, and pale brown. In the central portion of the lower pole of each lobe there was an irregular white zone of fibrous scarring measuring about 0.7 cm in diameter. One of these showed a few small irregular flecks of calcification.

Microscopic. Multiple sections taken through various portions showed an unusually varied picture. The majority of the acini were small and contained scant colloid. This was notched at the margins. The acini were lined by large cuboidal to columnar cells which had a faintly eosinophilic and partially vacuolated cytoplasm. The nuclei were small and vesicular. In addition there were several small nodules which were composed of acini which contained a granular basophilic material and which were lined by flattened faintly eosinophilic cells. Some of these cells, however, showed a transition to large eosinophilic cells resembling Hurthle cells. The stroma through most of these portions was scant, fibrous, and showed scattered foci of lymphocytic infiltration.

Multiple sections taken through the white zones noted in each lobe grossly showed in both of them a dense fibrous tissue. Within this fibrous tissue there were well formed gland spaces lined by amphophilic cells which varied from a cuboidal to a columnar in shape (Fig 1). These cells were more hyperchromatic than thyroid cells elsewhere. There was a marked papillary pattern to their arrangement at some points. In addition, the nuclei here were irregular in size, large, and showed prominent nucleoli. There were several small arteries and about these were small glands lined by atypical cells similar to the main cells in this portion and suggesting an invasion of perivascular lymphatics. There were irregular strands of glands lined by these atypical cells extending irregularly through both nodules (Figs 2 and 3).

The picture in the second portion was entirely different from that seen elsewhere in the gland. Here the gland spaces were atypical and there was great variation in the nuclei

THIOURACIL AND CARCINOMA OF THE THYROID

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THE marked proliferation produced in the thyroid by thiouracil has aroused in the minds of many the question of possible subsequent development of malignancies in the patients so treated. This marked proliferation alone with the high incidence of carcinoma in toxic nodular goiter has led Hinton and Lord to state that thiouracil is contraindicated in the treatment of toxic nodular goiter. Pertinent also is the experimental work of Belschowsky¹ who noted that rats fed thiourea and 2-acetaminofluorene developed adenomatous or anaplastic invasive tumors of the thyroid while either drug given alone did not produce such changes.

We have recently encountered a carcinoma in a patient with diffuse toxic hyperplasia of the thyroid who was treated preoperatively with thiouracil and iodine. Because of the possible carcinogenic activity of thiourea this case is reported here.

CASE REPORT

History—Mrs. W. H. D., a 56-year-old white woman, was first seen on Aug. 31, 1940, complaining of nervousness, anorexia, and a loss of forty-nine pounds in weight during the previous year. She had also noted increasing bulging of the eyes with impairment of vision. She had noted no increase in cold tolerance or heat intolerance. There were no gastrointestinal symptoms. The past history was entirely negative.

Physical Examination—Temperature was 98.6° F., pulse 105 to 120, respirations were 20, blood pressure 155/90. Body weight was 115 pounds. The general appearance of the patient was that of an emaciated nervous white woman with marked exophthalmos and appearing to be about the stated age. The ears, nose, and mouth were negative. The eyes showed marked exophthalmos with poor vision partially corrected by glasses. The neck showed a slight smooth fullness in the region of the thyroid. There was no bruit. The lungs were clear. The heart rhythm was regular but rapid and the sounds were of good quality. There were no murmurs. The pulse was forceful with a pulse rate varying at different times from 108 to 120. The abdomen and extremities were negative. The only positive finding on neuromuscular examination was a constant fine tremor of both hands which was exaggerated on extension of the arms and separation of the fingers.

Laboratory—Basal metabolic rate was +36, hemoglobin 13.6 Gm., red blood cells 4,100,000, white blood cells 7,000, with a normal differential count. The urine was negative.

Treatment and Progress (see Table I).—Treatment was begun on Aug. 31, 1940, with 0.6 Gm. of thiouracil each day for one week. On September 7 the basal metabolic rate was +22 with 64 per cent neutrocytes. Thiouracil

On September 14 the basal metabolic rate was +17,000 with 60 per cent neutrocytes. At

this time the weight was 116½ pounds and iodine was then increased to 0.4 Gm. daily and continued for six days. On September 20 the basal metabolic rate was +17, body weight 120 pounds, pulse 88, and the white blood cells 7,100 with 60 per cent neutrocytes.

treated gland and the gland of hyperthyroidism before iodine therapy has been pointed out by Graham² Shiner and Cohen³ and others. Broders and Parkhill⁴ also noted this hyperplasia and in addition reported the occurrence of mitoses in the epithelial cells of the acini. These findings serve to raise the question as to how far the growth stimulation produced by thiouracil will progress.



Fig. 9. Showing atypical cells extending throughout the tumor region (Phloxine methylene blue $\times 60$).

On the experimental side of particular interest is the work of Bielschowsky⁵ who noted that a combination of thiourea and 2 acetaminofluorene produced malignant tumors of the thyroid in rats. Wilson, Dekds and Cox⁶ first noted the carcinogenic activity of 2 acetaminofluorene and reported neoplasms occurring in many organs in rats fed this drug. Bielschowsky reported that when administered orally 2 acetaminofluorene produced carcinomas of the lungs, salivary glands, liver, pancreas and breast and leucemias and lymphosarcomas. None of these animals developed carcinoma of the thyroid. Bielschowsky then fed rats thiourea and again no tumors of the thyroid developed but when rats were fed thiourea and 2 acetaminofluorene anaplastic epithelial tumors of the thyroid developed. It thus becomes apparent that thiourea is capable of focusing the activity of at least one carcinogenic agent upon the thyroid.

which indicated that these lesions must be regarded as malignant. Blood vessel invasion was not noted but the cells were sufficiently atypical to warrant a diagnosis of malignancy. It is interesting that the change occurred in both glands which alone, with the papillary pattern suggested the possibility of the lesion having developed from previously existent papillary cystadenoma.

The picture throughout the remainder of the gland showed the marked hyperplasia encountered with thyroidal therapy and in addition the changes seen with preoperative iodine therapy.

Diagnosis. The diagnosis was diffuse toxic hyperplasia of the thyroid and papillary adenocarcinoma of the thyroid.



Fig. 1. Low power view of tumor zone. Note the marked difference between the more normal thyroid follicles on the left and the tumor throughout the center of the field and in the right lower corner.

DISCUSSION

The zones of tumor in this gland have all the characteristics of a malignant growth with considerable variation in cell and nuclear size and large nucleoli. The lesions were small and represent an incident finding for the clinical symptoms and the pathologic findings were primarily those of hyperthyroidism and not neoplasia.

The question then arises as to the possible relation of the neoplastic lesion to the preoperative thyroid therapy. The similarity between a thyroidal

incidence of carcinoma and that because of its carcinogenic potentialities thiouracil is contraindicated in the treatment of nodular goiter. Our case would lend support to this last hypothesis.

We cannot, of course, definitely state that the carcinoma developed in this individual because of the thiouracil therapy. There is one previous mention of carcinoma in a patient treated with thiouracil, this instance simply being listed by Moore and associates¹¹ in a table of cases treated preoperatively with the drug. There is no discussion of the case in their text. Future reports of similar cases will be necessary for any evaluation of the role of thiouracil in the development of carcinoma of the thyroid in man.

SUMMARY

A case of early carcinoma of the thyroid is reported occurring in a diffuse toxic hyperplasia of the thyroid which was treated preoperatively with thiouracil and iodine.

The question of the carcinogenic potentialities of thiouracil is raised but this will be determined by subsequent reports of similar cases.

We are indebted to Dr. A. P. Stout and Dr. A. K. Frantz of the College of Physicians and Surgeons, Columbia University, New York, N. Y., for reviewing this material and having the photomicrographs prepared.

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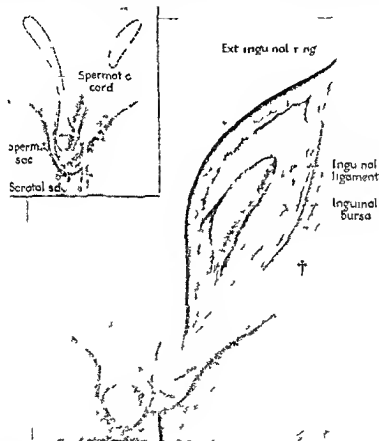
Of further pertinent interest in the role of thionin in the development of carcinoma in this case is the rarity of carcinoma in diffuse toxic hyperplasia of the thyroid. Ward¹ encountered only one case of carcinoma in 1900 in instances of diffuse toxic goiter, which agrees with the statistics cited by Boyd² to the effect that Wegelin encountered only 13 malignancies of the thyroid in 13426 autopsies in Berlin where the incidence of goiter is low. We therefore feel that the occurrence of the carcinoma in this case is unusual and that



Fig. 3. Another portion of tumor tissue showing more variation. Note the variations in cellular and nuclear structure (Ehloxins meth. len. blue $\times 40$).

in consideration of previous statistical studies the thionin may have played a part in the development of the growth. The fact that the gland showed a diffuse hyperplasia makes the occurrence of a carcinoma more unusual than if the gland had shown a nodular type of goiter. In nodular goiter the incidence of carcinoma is high, occurring 48 per cent in the series reported by Ward¹ and 72 per cent in that reported by Cole, Slaughter and Rossiter.³ Hinton and Lord⁴ pointed out that in this last series of 193 cases of nontoxic nodular goiter 17.1 per cent showed carcinoma and that in the group of nontoxic solitary nodules the incidence was 24 per cent. These statistics led them to the conclusion that all nontoxic goiters should be removed surgically because of the high

In regard to methods four patients were selected for careful study. During surgery the procedure was (1) to identify the inguinal bursa (2) to search for a cord of tissue below its blind end (3) to open the bursa in order to note any manifestations of a gubernaculum on its posterior aspect (4) to tag crucial portions of the bursa for the purpose of orientation in microscopic studies and (5) to remove the bursa plus attached strands of tissue (after



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freeing the testis. The surgical specimen thus obtained was fixed by placing it in 10% formalin solution. Portions of the specimen were passed through paraffin and sectioned at 6 μ . Certain sections of each portion were stained three methods being used (Mallory's triple, Gomori's and hematoxylin and eosin).

In anticipation of that which follows it was found that sections of a gubernaculum could not be identified in any of the microscopic preparations

MISCONCEPTION OF THE GUBERNACULUM TESTIS

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JOHN HUNTER (1786), who discovered the gubernaculum testis described it in part as "a substance which runs down from the lower end of the testis to the scrotum." A century later, Lockwood (1887, 1888) contributed to confusion when he reported that the lower end of it fans out to produce six strands of attachment (1) "to Scarpa's triangle," (2) to the pubis (3) to the root of the penis (4) to the scrotum, (5) to the perineum near the tuberosity of the ischium, and (6) to the sphincter ani.

Actually, in a fetus of the seventh lunar month, the upper end of the gubernaculum is attached to the tail of the epididymis (Wells, 1943). The lower end of it does not reach the scrotum but terminates at the bottom of the inguinal bursa of Klaatseh (1890). * This bursa is the sac that receives the testis and that originates by eversion of four layers of the abdominal wall (peritoneal, transverse, internal oblique, and external oblique). The bursa may be shelled out of the scrotum without tearing more than areolar tissue, as it may be also in the newborn (R H Hunter, 1926). Similarly, in the embryo of an adult man, the spermatic sac and the scrotal sac may be readily separated by blunt dissection† (see insert, Fig 1).

However, it is a common notion that in patients subjected to surgery for undescended testis it is possible to identify the gubernaculum as a definite "ligament" which extends from testis to scrotum or from testis to some non scrotal structure (Eisendrath, 1926, Thompson, Bevan, Heckel, McCarthy and Thompson, 1937, Abrahamson 1942 Bishop 1945 Schutt, 1945, Ormand Cothran and Singister, 1945).

The main object of the present study was to determine whether the gubernaculum could be identified in such patients. A second and related objective was to search for any discrete band of tissue which might account for the widespread opinion that the gubernaculum extends below that part of the inguinal bursa which normally becomes the spermatic sac.

— and research funds of the Graduate School

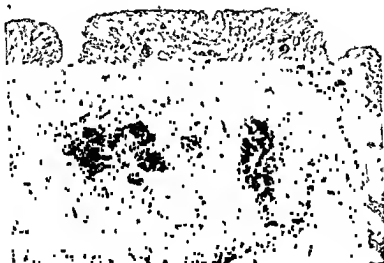
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On July 1, 1946, a left inguinal hernioplasty and orchiopexy were done under cyclopropane anesthesia. The hernioplasty was done according to the method of Ferguson (1899) and the orchiopexy as described by Wangenstein (1935).

Turning to observations in this case, the inguinal ring was visible as soon as the skin and tela subcutanea had been incised. A structure in the inguinal canal, subsequently identified as the testis, could be moved upward and downward by exerting manual pressure, but it would not pass through the external ring. The first indication of an inguinal bursa to appear was an indistinct outline of its fundus. Below the fundus, it was impossible to see or to palpate any cord of tissue that might be said to resemble a gubernaculum. Fig 1 illustrates the bursa as it appeared after strands of connective tissue had been stripped from its anterior wall and after a "ligament" of connective tissue had been "created" by blunt dissection (marked by dagger).



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When the bursa was opened, the testis could be seen through its thin covering of peritoneum (Fig 2). A gloved finger in the peritoneal sac (lining of bursa) could enter the abdominal cavity by passing through the patent orifice of the bursa*. Extending down from the tail of the epididymis was some unknown, retroperitoneal structure that elevated the peritoneum to produce a longitudinal ridge (asterisk). Aside from its narrowness, this ridge looked somewhat like that caused by a gubernaculum. It was tagged by means of thread then it and that part of the bursa distal to the testis and the attached "ligament" were excised as a unit and placed in fixing fluid.

In microscopic studies of transverse sections of the bursa, the four layers of its wall were observed. The most distinct ones were the peritoneal and the cremasteric. Since a gubernaculum, like a testis, is a retroperitoneal structure, the internal spermatic layer is

*This orifice should not be called the internal inguinal ring because the latter term is almost universally used for the purpose of designating a ring of transversalis fascia at the upper end of the inguinal canal. Incidentally most authors who report cases similar to ours use such general terms as hernial sac for referring to the four layered sac which contains the testis. The term inguinal bursa is useful for conveying the idea that the sac represents the anomalous persistence of a normal one of the fetus.

of the four surgical specimens. Therefore it was decided to present only one case, namely the one which turned out to be the most instructive. A clinical and surgical history of the patient is presented here.

CASE REPORT

D. B. (U. H. No. 765109) white male aged 12 years, was first seen at the University Hospitals on June 24, 1946. The main complaint was failure of descent of the testis bilaterally. In the summer of 1945 he had received a series of sixteen injections of gonadotrophic hormone (gonadotropin dose unknown) by his local physician without benefit. While receiving the injections a mass was noted in the left inguinal region which caused the patient no discomfort but which persisted.

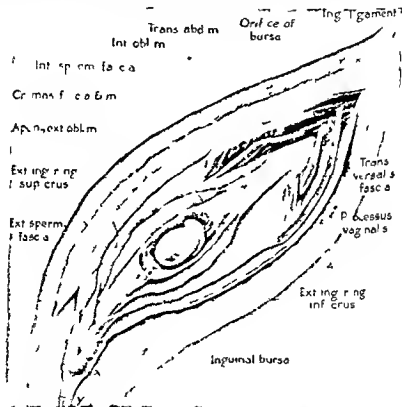


Fig. 2.—The left testis as it appeared after the bursa had been opened. The asterisk marks the site where a gubernaculum, if present, should be expected. The dotted lines (x and y) indicate a block of tissue that was sectioned serially and vertically (see text).

The family history was of interest in that the patient's father and two brothers each had unilateral failure of descent of the testis.

Physical examination on admission revealed a well nourished and well developed 12-year-old white boy who did not appear ill or in distress. The examination apart from bilateral cryptorchidism and an easily reducible left inguinal hernia was essentially negative. It was thought that the left testis could be felt high in the inguinal canal but the right testis could not be palpated at all.

observations support this view (1) in certain patients with undescended testis therapeutic injections of androgen are followed by descent (Hamilton 1941), (2) in primates the urine of pregnancy contains androgen (Hain 1939 Dorfman and Van Wageningen 1941) (3) in rodents during postnatal life, in injections of androgen cause rapid growth of the bursa (Wells²² 1944) (4) in unborn rats the size and number of the interstitial cells of Leydig may be increased experimentally by injecting gonadotropin under the skin (Wells²⁴ 1946) and (5) in experiments in which unborn rats are deprived of their testes or are subjected to this operation and then given pellets of androgen (subcutaneously) the data seem to indicate that the fetal testes produce a hormone (androgen) which accelerates the growth of such accessory reproductive organs as the seminal vesicles (Wells²³ 1946) We are not aware of any observations which indicate that the gubernaculum is influenced by hormones

There remains the related question as to why the testes had failed to enter the scrotum during puberty or to enter it in response to the therapeutic injections of gonadotropin Doubtless the answer is that by the beginning of puberty the external inguinal rings were too small and too unyielding to permit descent As mentioned this was true of the left ring at the time of orchiopexy Neither above this ring nor below it were there any bands of fibrous tissue that might have prevented a descent of the left testis

In conclusion we were unable to identify a gubernaculum in any of four selected patients who were subjected to orchiopexy The notion that in such patients it may be found below the infundus of the inguinal bursa is due to a misconception of it If present it should be on the posterior aspect of the bursa and in the internal spermatic layer

It is a pleasure to acknowledge our indebtedness to Dr Owen H. Wageningen who placed the patients at our disposal to Professor Edward A. Boyden who assisted in many ways but especially in planning the dissection and to Miss Dorothy N. Highby senior laboratory technologist who made the microscopical preparations

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the one which should be expected to contain it. Despite most careful search, no trace of a gubernaculum could be found.

Transverse sections of the tissue taggled by means of thread (asterisk Fig. 2) showed that the ridge of peritoneum observed during surgery was caused by blood vessels in the subperitoneal layer (tunica vaginalis communis or internal spermatic fascia). Fig. 3 illustrates this point.

A block of tissue including the fundus of the bursa and the upper part of the attached "ligament" (x y Fig. 2) was sectioned serially and vertically. The sections showed that the "ligament" consisted of areolar tissue and small blood vessels. Its upper end funneled out to become a uniform spray of filaments, the spray being most conveniently described by comparing it to that of a garden hose. These filaments united with the funnels of the bursa by blending with the outer layer (external spermatic).

In considering this case it is clear that the "ligament" created by blunt dissection should not be called the gubernaculum testes. On the posterior aspect of the internal spermatic layer of the bursa where a gubernaculum if present should be expected to be none could be found. Although these observations should not be taken to mean that in all patients with undescended testis a gubernaculum cannot be identified, they are evidence against the common notion that a place to look for one is below the bottom of the bursa.

The question arises as to whether the testis (left) had descended before birth and then had ascended after birth, a phenomenon which occurs normally in the rhesus monkey (Wislocki, 1933). This question cannot be answered because of a lack of records of pertinent observations on the patient during infancy. However, it may be pointed out that the presence of the bursa at the time of orchiopexy does not constitute evidence that at one time the testis had actually reached the scrotum because normally the bursa originates before the testis begins to descend. In a seven-month fetus in which one testis had already descended and the opposite one had not, the bursa on the side of non-descent had become a sizable structure (Wells, 1943).

Assuming that the left testis had not at any time reached the scrotum, might it be that agenesis of the gubernaculum had been the causative factor? This is most unlikely because at orchiopexy the testis was in the bursa and because it would seem that in the fetus the two main functions of the gubernaculum are to widen the orifice of the bursa and to steer the testis into it (Wells, 1944). It is more reasonable to suppose that the gubernaculum had existed before birth and had become unrecognizable after birth as in normal development.

As to why the left testis lay above the external inguinal ring, my view is that the gubernaculum had failed to pull it into the scrotum may be rejected because of a lack of acceptable evidence that normally the gubernaculum actually exerts traction upon the testis (Assner, 1928). In fact, in rodents severance of the gubernaculum is followed by descent of the testis in a large majority of the cases (76 per cent Wells, 1944).

The fact that this was a case of bilateral cryptorchidism points to hormones as the causative factor. It would seem that during pre-natal life the testes had failed to reach the scrotum because of failure of the androgen of pregnancy to cause the bursa to grow as rapidly as in normal fetuses. Several

observations support this view (1) in certain patients with undescended testis, therapeutic injections of androgen are followed by descent (Hamilton, 1941), (2) in primates the urine of pregnancy contains androgen (Hain, 1939, Dorfman and Van Wagenen, 1941), (3) in rodents during postnatal life, injections of androgen cause rapid growth of the bursa (Wells²² 1944), (4) in unborn rats the size and number of the interstitial cells of Leydig may be increased experimentally by injecting gonadotropin under the skin (Wells,²² 1946), and (5) in experiments in which unborn rats are deprived of their testes, or are subjected to this operation and then given pellets of androgen (subcutaneously), the data seem to indicate that the fetal testes produce a hormone (androgen) which accelerates the growth of such accessory reproductive organs as the seminal vesicles (Wells²² 1946). We are not aware of any observations which indicate that the gubernaculum is influenced by hormones.

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In conclusion we were unable to identify a gubernaculum in any of four selected patients who were subjected to orchiopexy. The notion that in such patients it may be found below the fundus of the inguinal bursa is due to a misconception of it. If present it should lie on the posterior aspect of the bursa and in the internal spermatic layer.

It is a pleasure to acknowledge our indebtedness to Dr. Owen H. Wangenstein who placed certain patients at our disposal to Professor Edward A. Poyden who assisted in many ways but especially in planning the illustrations and to Mrs. Dorothy A. Bligh, senior laboratory technologist who made the microscopic preparations.

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SOME OBSERVATIONS ON THE USE OF CURARE IN THE TREATMENT OF TETANUS

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CURARE until the past several years has been regarded as a pharmacologic curiosity rather than a therapeutic agent. Its clinical application has been attempted from time to time but because the available preparations were of variable potency and there appeared to be a narrow margin between the dose necessary for the desired therapeutic effect and that which caused respiratory failure its use in the treatment of disease was regarded as hazardous. The recent introduction of specimens of greater purity and standard potency has revived interest in the drug and stimulated investigation of its efficiency in diseases of the neuromuscular system. The activity of curare is due to various alkaloids but particularly to the presence of the illudoid di-tubocurarine a crystallizable substance. Crude curare contains hydrolyzable resins some of which give rise to undesirable side effects and toxic reactions. Through the efforts of Richard Gill in cooperation with the research departments of certain pharmaceutical concerns preparations of curare of standard potency devoid of noxious substances are now available. Two preparations generally employed for clinical use are Intocostrin which is the crude drug freed of resins and toxic substances and tubocurarine an aqueous solution of the active principle itself. Both are prepared so that a given specimen possesses standard potency. Intocostrin is widely used as an adjunct to general anesthesia to secure relaxation of the abdominal muscles. It is also extensively used to soften the convulsive phase in the metrazol treatment of psychoses. Scattered reports some favorable have appeared regarding its use in treatment of diseases of the neuromuscular system particularly when these diseases are characterized by spasticity and hypertonicity of the muscles.

One disease in which its use has been suggested is tetanus. The idea of using curare in tetanus is not new. Numerous reports have appeared in the literature from time to time some as early as 1850. On the whole the use of curare in the treatment of tetanus has up to the present time been disappointing and unsuccessful. The poor results have largely been ascribed to the uncertainty of composition and the variability of potency of the preparations of the drug. The possibility that the newer and more refined preparations such as intocostrin might be more successful than the older preparations leads us once again to observe its behavior in this disease.

It is obvious to one familiar with the pharmacology of curare and the pathologic physiology of tetanus that the drug can afford little more than symp-

somatic relief in this disease. Curare exerts its action by blocking impulses to skeletal muscle at the endings of the somatic nerves. Apparently it inhibits the action of acetylcholine at this point. Death from overdosage is usually ascribed to asphyxia from paralysis of the respiratory muscles. Recent experimental observations and clinical experience indicate that this premise is not strictly correct. Death has been known to occur from circulatory failure. In tetanus the usefulness of curare would be limited to overcoming the muscle spasm. The underlying cause of the disease would remain to be treated by antitoxin, penicillin or other measures.

A nicotine like action on the autonomic ganglia may also be observed. However, this action appears to be of little concern clinically because the dose necessary to cause it is larger than that which causes paresis of the skeletal muscles. In addition a histamine like action is occasionally encountered.

The following are some observations made in five patients in whom the diagnosis of tetanus was established.

METHOD OF STUDY

The aqueous solution of curare, known as Intocostrin* containing twenty units of standard curare per cubic centimeter, was used undiluted in all cases. Resuscitating equipment for artificial respiration and for administering oxygen was available at the bedside at all times. Curarization was supervised by a physician member of the anesthesia department who remained in constant attendance throughout the entire therapy. Prostigmine which to a certain extent antagonizes the curare action was held in readiness for intravenous administration in the event of overdosage. The recommended dose of one half unit per pound of body weight was computed in each case and this amount was not exceeded at any one time.

CASE REPORTS

CASE 1—A 25 year old colored woman complaining of stiff neck and trismus of two days duration was admitted to the hospital. There was no history of trauma. The patient

was in a good state of nutrition and appeared to be mentally clear. Physical

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diagnosis of tetanus was made.

Upon admission tetanic antitoxin was administered 1100 units intravenously and 200000 units intramuscularly. In addition phenobarbital 1/2 gr. was given intramuscularly every four hours. Eight hours after admission the anesthesiologist was consulted regarding the use of curare to alleviate physical exhaustion from the muscle spasm. Intocostrin was administered intravenously at the rate of 10 units per minute until 60 units had been injected. An average of two minutes was allowed to elapse between the injection of each cubic centimeter of solution. The jaw gradually relaxed over a period of five minutes from the time the injection was started and the rigidity of the neck diminished. The abdominal muscles remained rigid however and the extremities were still hypertonic. The reflexes decreased in activity but remained active. After three minutes an additional 20 units of Intocostrin were administered slowly over a period of two minutes.

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This was followed by relaxation of the back and abdominal muscles. The muscles of the neck and jaw in the meantime became completely flaccid. After several minutes more the amplitude of thoracic excursions became markedly diminished. The diaphragm still remained active. Soon the diaphragmatic movements diminished and cretaceous of the mucous membranes and nail beds appeared. There was definite embarrassment to respiration necessitating the use of oxygen by mask. The pulse and blood pressure remained unchanged, however. Pulmonary ventilation became further embarrassed by obstruction caused by relaxation of the tongue. The tongue was supported by a rubber oral airway. The patient appeared drowsy, apathetic, did not respond to stimuli, and was unable to talk or swallow. The flaccidity gradually lessened, and diaphragmatic activity began to return. Within thirty minutes the trismus and rigidity of the back and abdominal muscles had returned. The status of the muscular system appeared no different than before curarization. The patient was again aware of her surroundings and was alert. Pulse and blood pressure did not vary significantly during the entire period of curarization.

Forty five minutes after the completion of the injection of the first dose, 80 units were again administered intravenously over a period of twelve minutes. The sequence of events was similar to those following the first dose. However, the state of muscle relaxation and flaccidity lasted only twenty minutes this time. Eighty units were then administered intramuscularly in one dose. The flaccidity gradually reappeared and was maximal in fifteen minutes, it lasted approximately thirty minutes.

During the relaxation induced by the second and third injection, considerable mucus and saliva accumulated in the pharynx. The patient was unable to swallow these secretions because of the loss of control of the pharyngeal muscles and the muscles of deglutition. The secretions interfered with the airway unless frequent suctioning was practiced. This appeared to be an objectionable feature of the therapy as it markedly increased the hazard of asphyxia in the face of the diminished ventilation due to paresis of the intercostal muscles and diaphragm. In view of the fact that a partial or graded response could not be obtained and the amount necessary to obtain relaxation caused complete curarization, no further use of the drug was attempted and therapy was continued by means of sedatives in conjunction with the antitoxin. The temperature came down by lysis, the muscle spasm gradually disappeared and the patient left the hospital free of symptoms after three weeks.

CASE 2.—A 20 year old colored man was admitted to the hospital complaining of pain in the jaws, stiffness of the extremities, and inability to open the mouth for ten days. Symptoms developed several months after he lacerated the right index finger. Physical examination revealed trismus, the classical risus sardonicus, generalized rigidity of the back and neck muscles and opisthotonus. Temperature was 104° F and he was semicomatose. No significant changes were noted in spinal fluid and urine or blood studies. A diagnosis of tetanus was made.

One hundred thousand units of tetanus antitoxin were administered intravenously and 40,000 intramuscularly upon admission. Phenobarbital, gr 3 was given intramuscularly every four hours. Eight hours after admission, intocortin was administered intravenously at the rate of 20 units per minute. Forty units caused a relaxation of the jaw and disappearance of the trismus. This amount was augmented in an effort to relax the muscles of the abdomen and lower extremities. Seventy units were required to effect relaxation of the muscles of the extremities. The intercostal muscles by this time lost their activity and respiration became diaphragmatic. The power of deglutition and phonation was lost and saliva and mucus accumulated in the pharynx. As in the previous case, the decrease in pulmonary ventilation caused anoxemia which necessitated the use of oxygen. The effect of the curare lasted approximately forty minutes after which time the spasticity and hypertonicity of all the muscles returned and appeared to be of the same intensity as before curarization. In view of the fact that the dose necessary to cause relaxation of the extremities was sufficient to cause almost complete cessation of the respiratory movements, no further curarization was attempted at this time. Ten hours later the patient was completely exhausted from the marked spasticity. It was decided to give the drug another trial. The lower extremi-

tomitic relief in this disease. Curare exerts its action by blocking impulses to skeletal muscle at the endings of the somatic nerves. Apparently, it inhibits the action of acetylcholine at this point. Death from overdosage is usually ascribed to asphyxia from paralysis of the respiratory muscles. Recent experimental observations and clinical experience indicate that this premise is not strictly correct. Death has been known to occur from circulatory failure. In tetanus the usefulness of curare would be limited to overcoming the muscle spasm. The underlying cause of the disease would remain to be treated by antitoxin, penicillin or other measures.

A neuromuscular action on the autonomic ganglia may also be observed. However, this action appears to be of little concern clinically because the dose necessary to cause it is larger than that which causes paralysis of the skeletal muscles. In addition, a histamine like action is occasionally encountered.

The following are some observations made in five patients in whom the diagnosis of tetanus was established.

METHOD OF STUDY

The aqueous solution of curare, known as Intocoxtrin,* containing twenty units of standard curare per cubic centimeter, was used undiluted in all cases. Resuscitating equipment for artificial respiration and for administering oxygen was available at the bedside at all times. Curarization was supervised by a physician member of the anesthesia department who remained in constant attendance throughout the entire therapy. Prostigmine which to a certain extent antagonizes the curare action was held in readiness for intravenous administration in the event of overdosage. The recommended dose of one-half unit per pound of body weight was computed in each case and this amount was not exceeded at any one time.

CASE REPORTS

CASE 1—A 25-year-old colored woman coming with stiff neck and trismus of two days' duration was admitted to the hospital. There was no history of trauma. The patient was well developed in a good state of nutrition and appeared to be mentally clear. Physical examination revealed fever (101° F), trismus, rigidity of the neck and abdominal muscles and hyperlordosis of the muscles of the extremities. No puncture or other wound could be demonstrated. Blood urine and spinal fluid examinations revealed nothing significant. A diagnosis of tetanus was made.

Upon admission tetanus antitoxin was administered 10,000 units intravenously and 20,000 units intramuscularly. In addition phenobarbital gr. 15 was given intramuscularly every four hours. Eight hours after admission the anesthesia department was consulted regarding the use of curare to alleviate physical exhaustion from the muscle spasm. Intocoxtrin was administered intravenously at the rate of 20 units per minute until 60 units had been injected. An average of two minutes was allowed to elapse between the injection of each cubic centimeter of solution. The jaw gradually relaxed over a period of five minutes from the time the injection was started and the rigidity of the neck diminished. The abdominal muscles remained rigid however and the extremities were still hyperlordotic. The reflexes decreased in activity but remained active. After three minutes an additional 20 units of Intocoxtrin were administered slowly over a period of two minutes.

*Supplied by F. R. Squibb & Sons, New York, N. Y.

intramuscularly for four days. During this time, in spite of heavy sedation with barbiturates and the use of tetanus antitoxin, the muscle spasm appeared to increase in severity and became more generalized. On the fifth day, it was decided to alleviate the spasm with curare. Intocostrin was administered intravenously at the rate of 10 units per minute. Sixty units in all were given at this time. The jaws slowly relaxed. Within five minutes, after completion of the injection, the effect of the drug appeared to be well established. The abdominal muscles and muscles of the lower extremities remained rigid, however. An additional 20 units were given. The ankle clonus, which had persisted, now disappeared, but the powers of deglutition and phonation disappeared also. Thoracic movements became depressed although the diaphragm remained active. Saliva and secretion accumulated in the pharynx in spite of the administration of 0.5 mg atropine intravenously before curarization. Forty minutes after the initial administration, the muscle tone began to return. In fifty minutes the muscles appeared to be as spastic as before curarization. Blood pressure and pulse varied little throughout the entire procedure. An additional 60 units were administered intravenously in the same manner but at a slower rate than the previous injection. The time of administration was exactly one hour after the first injection. Within five minutes, the relaxation was complete. The intercostal muscles were inactive, the powers of deglutition and phonation were absent and the extremities were relaxed. Saliva and secretions appeared again in copious amounts. One hour later, the tone of the muscles began to return. The patient remained quiet. The dose was not repeated as in the previous cases because the amount necessary to cause an appreciable loss of muscle tone caused respiratory depression. Gradually the patient became restless. Five hours later there was marked excitement and intense spasticity of the muscles. Sixty units were again administered intravenously in the same manner as previously described. The behavior was similar to that after the previous injection. The response lasted fifty minutes this time. The dose was repeated again and similar results were obtained. Each administration was followed by marked respiratory depression in this subject. In view of this and the experience with Case 3, curarization was discontinued.

CASE 5.—A 24 year old colored man was admitted to the hospital complaining of pain upon swallowing. The day before admission, he developed pain and stiffness in the jaws. Physical examination revealed trismus, stiffness of the neck muscles, and rigidity of the abdominal muscles. A diagnosis of tetanus was made. He was given tetanus antitoxin, both intramuscularly and intravenously, and phenobarbital at four hour intervals as in the previously described cases. Approximately twenty four hours after admission curarization was attempted.

Intocostrin was administered slowly intravenously at the rate of 10 units per minute. Eighty units were necessary to produce any notable effects. The jaws slowly relaxed. Within four minutes after completion of the injection the effect of the drug appeared to be well established. The intercostal muscles became progressively less active. The diaphragm, however, remained active.

Artificial respiration was instituted when completion of the injection of the curare was complete. The pulse remained unaltered. There was no notable change in blood pressure. Diaphragmatic activity began to return twenty minutes later but because movements were ineffective in maintaining adequate pulmonary ventilation the artificial ventilation was continued. The intercostal activity became fully established one and one half hours later. Power of deglutition returned after two hours. It seemed unwise in the face of the response obtained to repeat the administration of the drug.

DISCUSSION

Although one cannot pass upon the merits and demerits of curare in the treatment of tetanus from the experience of the foregoing cases, it is obvious that the therapy as conducted in the patients was not without hazards and pos-

ties were rigid. Seventy units of intocostin were again administered intravenously in divided doses over a period of five minutes. As before, complete paralysis of the muscles of the cranial, cervical, and spinal segments was obtained before any appreciable loss of tone of the muscles of the extremities was apparent. The effect lasted thirty minutes. The hypertonicity and spasticity reappeared and returned to apparently the same intensity as before the administration of the drug. Seventy units were again administered, but this time intramuscularly in a single dose. Within fifteen minutes the muscles of the upper extremity were completely flaccid. The powers of deglutition and phonation were gone, there was a notable diminution in thoracic and diaphragmatic activity. The lower extremities continued to be spastic at all times, however. Forty five minutes after the administration of the drug hypertonicity and rigidity reappeared in the muscles of the head and neck. No further attempt at curarization was made because it was obvious that the dose necessary to relax the lower extremities in this case could be obtained only by complete curarization and respiratory paralysis. Treatment was continued with hypnosis and the patient recovered.

CASE 3.—A 63 year old colored woman was admitted to the hospital complaining of stiffness of the jaws and rigidity of the muscles for ten days. The portal of infection was a puncture wound caused by a splinter in the right heel. Details of the history were vague. Tremor and rigidity of the neck and back muscles were pronounced. She appeared to be well nourished and alert. With the exception of the neuromuscular findings, no abnormalities were noted upon physical or laboratory examinations. A diagnosis of tetanus was made.

She was given tetanus antitoxin, 60,000 units intravenously and 40,000 intramuscularly. In addition, phenobarbital, gr 1½, and scytal, gr 1½, were given intramuscularly every four hours during the first day. Oxygen by nasal catheter was also given. Twenty four hours after admission, because there appeared to be little change in the neuromuscular status, curare was requested. Intocostin, 40 units, was given slowly over a period of several minutes. Ptosis, heaviness of the lids, and relaxation of the muscles of the head and neck gradually appeared. The muscles of the abdomen became relaxed and the intercostals

anesthesia machine. During this period, the airway became obstructed with mucus as in the previous cases, had accumulated in the pharynx. This was easily and quickly removed by applying suction. During this interval, however, the pulse became slow, weak, and at one time imperceptible. Blood pressure was not recorded at this time. Prostigmine (2 cc of 1:2000 solution) was given intravenously to antagonize the curare effect. After an estimated period of five minutes, the pulse became perceptible, then stronger, soon regaining its former quality and becoming of good volume. Diaphragmatic breathing became reestablished as the effects of curare wore off. The spasticity and rigidity of the muscles returned. One hour after the administration of the drug respiration became labored and jerky and the pulse became irregular and finally imperceptible. Severe gasping respiration and respiratory failure followed. Artificial respiration was immediately instituted and continued for approximately fifteen minutes. The heart sounds were inaudible, the pulse was not palpable, and blood pressure was unobtainable. The mucous membranes were cyanotic, pupils widely dilated and skin cold and clammy. Metrazol was given intravenously. This was followed by intracardiac adrenalin. After several more minutes the futility of employing further resuscitative measures was recognized and the patient was pronounced dead. Permission for a postmortem was not granted. It was impossible to determine from the sequence of events whether death was due to the effects of the curare, either directly or indirectly, or to some other factor incidental to curarization. It was our feeling that indirectly it was due to curarization.

after receiving
antitoxin

In most instances the drug was given while the patient was receiving barbiturates. On three occasions in three of the cases the sedation was withheld and the curare used alone. No appreciable difference was observed.

SUMMARY

Curare (mivococarin) was given to five patients in whom the diagnosis of tetanus was made for the purpose of alleviating convulsions and muscle spasm. Relief from the spasm was not obtained until the dose which caused almost complete curarization was given. The response was fleeting, lasting in most instances twenty or thirty minutes after which time it was necessary to repeat administration of the drug. In addition respiratory depression and obstruction were avoided with difficulty. One patient died one hour after administration of one single dose of curare which had been followed by respiratory and circulatory failure. Although the cause of death was not determined in this case it was believed to be caused by the curare.

The writers wish to acknowledge the assistance of D. D. A. Ponon Vega, resident in anesthesia at the Charity Hospital.

sesses certain drawbacks. First and foremost is the objection that the action of the drug was of short duration. Repeated doses were necessary at frequent intervals to maintain a sustained effect. This would not be a drawback if almost complete curarization had not followed each attempt to obtain the degree of muscle relaxation deemed to be of clinical value. When curare is used as an adjunct to inhalation anesthesia the loss of muscle tone appears to be in proportion to the amount of drug used. This graded response was not obtained in these patients. Instead the effect appeared to be abrupt in onset rather than gradual and the muscles became flaccid shortly after the loss of muscle tone became apparent. Even though the curare was administered slowly in divided doses the decrease in muscle tone was not apparent until the amount which caused flaccidity of muscles had been administered. Moreover the various groups of muscles were not affected simultaneously. The quantity of drug sufficient to relax the muscles of the head and neck did not necessarily affect the muscles of the lower back or abdomen. The fact that curare affects structures innervated by the cranial and cervical nerves before those innervated by spinal nerves was well demonstrated by these patients. The dose necessary to relax the more resistant groups of muscles innervated by the lower spinal nerves caused paralysis of the muscles supplied by the cranial nerves. The secretion of saliva and mucus continued, but due to the loss of power of deglutition accumulated in the pharynx. The pharyngeal muscles became relaxed the tongue slipped backward into the pharynx and together with the mucus caused partial obstruction to the airway. Pulmonary ventilation was further embarrassed by paresis of the intercostal muscles. Respiration invariably was gasping and jerky. The possibility of obstruction coupled with diminished ventilation was a hazard which was experienced with each administration of the drug. Theoretically respiratory failure should be adequately cured for by artificial respiration. However tetanus is a serious disease in which considerable stress is placed upon the respiratory and circulatory systems by the rigidity and convulsive spasms as well as the infection. Respiratory failure under these circumstances can be disastrous. Furthermore recent experimental studies in dogs indicate that death occurs after protracted use of curare even in the face of adequate pulmonary ventilation.* Presumably it is the result of circulatory failure. In view of the hazards involved constant attendance of the physician directing the therapy is mandatory. Although this is not too much to ask to save a life it often happens that such arrangements are not always possible.

The suggestion has been made that the drug be administered in small doses at less frequent intervals without attempting to overcome completely the spasm and obtain "normal" muscle tone. This technique has been employed in various types of myotomas and spastic diseases with some degree of success. However, the promptness with which rigor, trismus and other manifestations of hypertonicity returned as the effects of the drug diminished seems to preclude this as a possibility.

*Perlstein, M. A. and Weinglass, A. Fatal Effects of Prolonged Complete Curarization
Am. J. Dis. Child. 67: 360, 1944.

bronchi, bronchioles, atria, infundibula, or alveoli, and the nature of the epithelium may be profoundly modified by the increase in the size or by the ballooning of the cyst as well as the presence of infection.

According to Miller⁴ the manner in which a bleb is formed is similar to that which takes place in an interstitial emphysema, namely, a rupture of the wall of an alveolus which allows the air to escape into the alveolar layer of the pleura. This occurs at a point where, from some cause, the elastic fibers in the alveolar wall have given way, possibly from having been stretched to the breaking point. The air extends along the pleura in the same manner that a dissecting aneurysm extends along the wall of an artery. He also found a well marked emphysema in every case in which emphysematous blebs occurred.

In the case of a bulla the alveoli are first dilated then atrophy and rupture of the alveolar walls take place with a gradual formation of a bulla of greater or less size which communicates with a bronchiole or a larger division of the bronchial tree. In the case of a bleb the pleura is separated by the air from the underlying alveolar walls. In bulla formation the pleura retains its connections with the lung although the alveoli beneath it give rise to a bulla through rupture and fusion.

Grossly in the first type the pleura gives the sensation of a thin membrane which slides freely over the surface of the underlying substance. In the case of a bulla, it is not movable and the underlying space gives the impression of an air filled cavity.

Although the emphysematous bleb and bulla have been included in the group of pulmonary cysts they actually are two distinct entities. The wall of the former pathologic condition is lined by the surrounding alveoli and there is no true epithelial lining while the latter has a definite bronchial epithelium. The bulla can be considered best as an advanced stage of a localized pulmonary emphysema.

Obstructive processes of the bronchi caused by either intrinsic or extrinsic lesions will produce a hyperinflated bulla. As a result of a check valve mechanism however, the affected segment becomes blown up with air so that the bulla may reach huge dimensions which may rapidly increase or diminish in size and not infrequently disappear. Because of this valvular mechanism, constant intracavitary positive pressure may develop, giving rise to a picture which is described by many as *pneumatocele*.

CLINICAL PICTURE

Since emphysematous blebs and bullae are frequently associated with marked emphysema the clinical picture may be that of the latter condition only. The symptomatology however, depends on the size, location, valvular mechanism, condition of contiguous lung parenchyma and changes that may take place in the intrathoracic pressure. Infection is rarely seen and plays no important role in masquerading the disease, unlike cysts of other types which are prone to infection and frequently cause symptoms of pulmonary suppuration.

PULMONARY CYSTS

SPECIAL REFERENCE TO SURGICAL TREATMENT OF EMPHYSEMATOUS BLEBS AND BULLAE

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PULMONARY cysts, a pathologic entity that includes abnormal localized distentions of the various portions of the tracheobronchial tree and other discrete sacs originating from the interstitial portion of the lung are found in increasing numbers today because of the wider use of routine roentgenologic examinations of the thorax.

Bartholin in 1687, reported the first recognized case. Since that time many have been reported. Koontz¹ in 1925 reviewed the medical literature and found presentations of 105 cases and in 1937 Sehenek² found reports of 381 cases.

However the term "pulmonary cyst" has been used to designate a wide variety of pathologic entities, thereby creating confusion concerning the clinical terminology. Various pulmonary lesions have been included in this group: congenital pulmonary cyst, cystic bronchiectasis, epithelized cavities following pulmonary suppuration, pneumatocele (localized alveolar or lobular atelectasis), chronic interstitial pneumonia with emphysema, emphysematous bullae, and pulmonary blebs.

It therefore, becomes evident that when one mentions pulmonary cyst strong consideration should be given to its etiology, pathogenesis, and clinical picture rather than to discuss pulmonary cysts as a homogeneous group. Emphysematous blebs and bullae have come to our attention on occasion and unlike congenital cystic disease of the lung, little has been written concerning their surgical management.

It is therefore the purpose of this paper to present five cases: three emphysematous bullae, one subpleural bleb, and one chronic interstitial pneumonia with emphysema, four of which were treated by conservative surgery and one by lobectomy.

ETIOLOGY AND PATHOLOGY

Although the precise mechanism of the genesis of pulmonary cysts is still unknown, it is generally admitted that they originate either from a developmental error or anomaly. Boyd³ stated that there is such a great difference of opinion as to their pathogenesis that dogmatic statements are most unwise but there are three probable origins: (1) congenital bronchiectasis, (2) dilatation of lymphangiomatous spaces, and (3) cyst formation in aberrant lung tissue or vestigial structures. The wall of the cyst may have the characteristics of

ity the cyst which is under pressure will immediately herniate through the pleural rent while the normal lung tissue will collapse because of the pneumothorax. The cyst may then increase in size with the administration of endotracheal positive pressure. Attempts to decompress the cyst manually are usually futile, proving the presence of a one way valve mechanism. The cyst wall may be uni or multilobulated. Not infrequently discrete emphysematous

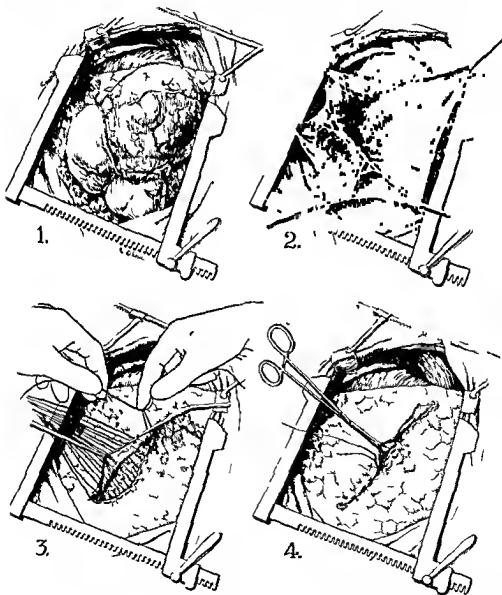


Fig 1—1 Pulmonary cyst visualized through operative incision 2 closing suture over bronchial orifice 3 imbricating sutures in visceral pleura 4 final closure with interrupted black silk

Many cases are symptomless and unrecognized for long periods of time when the lesions are not sufficiently large. Often pulmonary blebs and bullae acquire large dimensions with marked compression of the surrounding lung and displacement of the mediastinum causing respiratory embarrassment. Dyspnea is then a prominent symptom the degree of which depends upon the patient's activity or exertion. The difficulty in breathing is not infrequently in the form of wheezing. Cough, expectoration or pain in the chest are frequent complaints. Occasionally the sputum may be blood streaked. Cough associated with wheezing may suggest a diagnosis of bronchial asthma.

Not infrequently a spontaneous pneumothorax resulting from a rupture of a pulmonary bleb or bulla is indicative of this condition as has been clearly demonstrated in patients reported by Oechsli and Miles.*

RADIOLOGIC FEATURES

Röntgenographic study presents the only evidence in the diagnosis of pulmonary bleb and bulla. The lung field shows a peculiar variation from normal. The shadows cast by these structures are usually circular or ring shaped, sometimes linear, vacuolated in type simulating bronchiectasis. They appear in the roentgen plate as a large area of increased brilliancy in the midst of which a few lung markings can be seen. The border of these annular shadows is represented by a fine hairlike thin and sharp area of increased density which differentiates them from the walls of a congenital cyst which are rather coarse and often finely frayed out.

A tension or localized pneumothorax can frequently be mistaken for either a bleb or bulla because both conditions show an area of increased brilliancy and lack of normal lung markings. However in a large emphysematous bulla some compressed pulmonary tissue can always be seen either in the apex of the lung or in the costophrenic angle. Another differential feature is that in tension pneumothorax the lung collapses toward the hilus where it forms a prominence at its root.

TREATMENT

As previously mentioned emphysematous blebs and bullae under certain conditions such as check valve mechanism with obstruction to the egress of air, will balloon out and acquire large dimensions. The mechanical effect upon respiration and circulation will then cause incapacitating dyspnea. Pulmonary blebs and bullae even when large can be asymptomatic and only discovered by x-ray examination. They frequently will disappear spontaneously. These patients are not candidates for surgery no more than when they constitute only a part of generalized pulmonary fibrosis and emphysema.

The five patients that we report have all been operated upon because of respiratory distress to the degree of incapacitating them from leading a normal life.

OPERATIVE PROCEDURE

Operation can be performed under local paravertebral block with endotracheal intubation or under general anesthesia. Upon opening the pleural cavity

absence of breath sounds over the lateral and posterior portions of the lung. Roentgenogram (see Fig 2, A) of the chest on Dec 19, 1944, showed a thin walled, clear area at the left base which extended from the anterior to the posterior chest wall but did not include the costophrenic angle. There was no fluid present in the pleural cavity. The markings in the adjacent lung were somewhat thickened and, except for this, the lung appeared clear elsewhere. The mediastinum was displaced slightly toward the right and the left diaphragm was somewhat elevated, probably as a result of the megacolon. Bronchoscopy revealed an upward displacement of the left upper lobe bronchus with narrowing of the lower lobe due to extrinsic pressure. At operation Dec 20, 1944, excision of emphysematous bleb was done. During operation many subpleural emphysematous blebs in the dorsal segment of the lower lobe and one very large in the lingular segment of the upper were seen. The lingular segment had a complete fissure line, creating a separate lobe.

Microscopic Diagnosis—Microscopic diagnosis was emphysematous lung tissue consistent with subpleural bleb.



Fig 2 (Case 2)—A, Preoperative roentgenogram showing pulmonary cyst. B, postoperative roentgenogram, showing absence of cyst with re expansion of remaining lung tissue.

Comment—This patient was referred to us because of progressive shortness of breath which prevented him from doing his work. Intrathoracic pressure symptoms were present as shown by roentgenogram and bronchoscopy. The operation relieved the patient of the symptoms. Follow up x ray picture (Fig 2 B) showed re expansion of the remaining lung with absence of emphysematous changes.

CASE 3—I B, a 22 year old student nurse was admitted to the hospital September, 1944, complaining of fatigue and some shortness of breath for quite some time, but these symptoms were not bothersome until two months before at which time she complained of progressive dyspnea, slight cough productive of two ounces of mucoid sputum daily, associated with pressure sensations and soreness in the lower left chest region. During the two months previous to admission, she had noticed that the left costal margin was beginning to flare out. She was then admitted to the Boston City Hospital where a diagnosis of spontaneous pneumothorax was made. Upon reviewing roentgenograms taken one and one-half years before, the

changes can be seen in the periphery of the remaining lobes. One or more segments may be involved. The capsule is thin, glistening, and translucent. Upon opening the air-containing cavities, loose strands of fibrous tissue are encountered traversing the walls. The communicating bronchioles cannot always be found, even with the aid of increased intrapulmonic pressure. However increased pressure delineates with relative accuracy the margins of the healthy lung. Bronchiolar openings, when seen, are closed individually with mattress silk sutures. Through and through mattress sutures are next placed at the base of the cyst through healthy lung tissue in order to obtain an airtight repair. At this time, saline solution is poured into the open cyst and the anesthetic is required to increase the intrapulmonic pressure so that air leaks may be detected and if present, are repaired. The walls of the cyst are then excised down to the previous suture line and the lung surface is pleuralized by suturing the edges of the removed cyst with interrupted silk. Little or no hemorrhage is encountered. Emphysematous lobules are sometimes present in a pedunculated form and can be easily removed by placing mattress sutures through their pedicles. The lung is again expanded for further detection of air leaks. The pleural surfaces are then rubbed with dry gauze in order to produce an obliterating pleuritis. A drainage tube is finally placed in the pleural cavity which is kept under negative suction for forty-eight hours to facilitate a rapid re-expansion of the remaining lung and obliteration of the pleural space.

CASE REPORTS

CASE 1—J. H. a 36-year-old man was a motorman. He had a history of chronic rough progressive shortness of breath and wheezing for the past five years. Shortly previous to admission the patient coughed and expectorated about two ounces of mucopurulent sputum and had pain in the right chest associated with marked dyspnea and wheezing. Examination of the chest revealed marked limitation of motion on both sides and an emphysematous type of chest. Over the region of the right upper lobe, breath sounds were very distant. X-ray examination on Sept. 4, 1943, revealed the left lung to be apparently normal. The upper right lung field showed an increased brilliancy and a marked reduction in pulmonary markings which suggested a large thin-walled bleb or cavity. The right upper lobe was displaced toward the diaphragm as a result of the air-containing cavity. At operation on Dec. 3, 1943, excision and repair were done. A giant air-containing cyst was found in the right upper lobe filling approximately one-third of the volume of the right hemithorax. Posterior to the cyst four small bullae were seen.

Microscopic Diagnosis—Microscopic diagnosis was compatible with bullous emphysema.

Comment—This patient was treated for asthma for many years because allergy tests proved him to be sensitive to house dust. Following operation, the patient was markedly relieved of dyspnea and wheezing. X-ray follow-up revealed a completely re-expanded upper lobe with no evidence of emphysematous changes.

CASE 2—L. H. a man aged 58 years, a clerk, was admitted to the hospital December, 1944. Up until three years before, the patient was in apparent good health. At that time while riding in a car, he was seized with a paroxysm of coughing and complained of marked shortness of breath which was progressive. There was no history of expectoration, hemoptysis, or wheezing. He had sinus trouble for several years. He also had a double inguinal hernia repaired and megacolon, still present at the time of admission. Upon physical examination no abnormalities were found in the right lung. In the left lung there was an

the left side which had been present for three years. Roentgenogram taken one year before admission revealed a large, air-containing cyst in the left lower side of the chest. Anterior view (see Fig 3, A) upon admission revealed decreased density throughout the entire lower half of the left lung. Throughout this area many fibrotic strands were present, giving rise to a cystlike appearance. Lung markings in the superior portion of the emphysematous bleb appeared to be quite close together. The upper third of the lung showed no abnormality. The impression was that of emphysematous bleb involving the lower one half of the left lung. Upon comparing both views, taken one year apart, a definite increase in the size of the cyst was noted. Physical examination revealed hyperresonance and absence of breath sounds in the left lower thoracic area. While in the hospital the patient developed an episode of coughing, wheezing, and cyanosis which simulated a typical bronchial asthma attack. At operation Aug 17, 1945, excision and repair were done. When the pleural cavity was opened a huge, balloon cyst immediately herniated through the opening indicating the high intracavitary positive pressure.

Microscopic Diagnosis.—Microscopic diagnosis was emphysematous lung tissue, consistent with bulla.

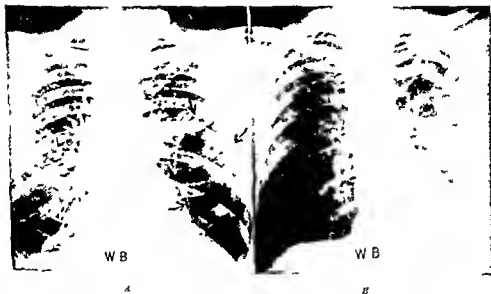


Fig 3 (Case 5).—A, preoperative roentgenogram showing pulmonary cyst; B, postoperative roentgenogram showing absence of cyst with expansion of remaining lung tissue.

Comment.—This case was interpreted as bronchial asthma and treated accordingly without benefit. The increase in the size of the pulmonary lesion and displacement of the mediastinum demonstrate the increase in positive intracavitary pressure which results from the check valve mechanism. Postoperative roentgenogram (Fig 3, B) reveals complete re-expansion of the lobe with disappearance of the emphysematous area. Patient has returned to work with no incapacitating symptoms.

CONCLUSIONS

1. Five cases of pulmonary emphysematous cysts: three bullae, one bleb, and one chronic interstitial emphysema involving the entire left lobe, are presented.

same radiologic picture was found which was later interpreted as a congenital cystic formation of the left lobe. Examination of the left side of the chest revealed a slightly prominent left costal flare. Percussion note was hyperresonant and breath sounds were almost absent over the left lower lobe area. Breath sounds were also high pitched and slightly suppressed over the left upper lobe. Bronchogram revealed a distorted left lower lobe bronchus with crowding of the bronchial branches. At operation on July 27, 1944, the lower lobe was found to be ballooned out, especially in the basilar segment. No anthracotic pigment could be seen in that segment, in contrast to the superior segment, which presented normal pigmentation. Diffuse hyperinflated lobules were found rather than one thin walled, large ballooned cyst as was suggested by the roentgenogram. A left lower lobectomy was performed. The gross specimen revealed about 90 per cent of the lobe to be made up of tensely distended lung conforming to the shape of the chest wall. This portion was smooth glassy tan, light pink yellow, and was soft and spongy in consistency. At the apex and along the anterior portion of the medial aspect, there was a strip of gray purple, noncrepitant atelectatic lung tissue present. The cut surface revealed widespread spongy lung parenchyma involving about 95 per cent of the lobe. This segment consisted of diffusely dilated alveolar sacs which measured to 0.5 cm across.

Microscopic Diagnosis—Microscopic diagnosis was marked emphysema with peripheral atelectasis.

Comment—Although no single, large bulla or bleb was found the x ray shadows were mistaken for a pneumothorax. The hyperinflated lobules caused the pressure symptoms and progressive dyspnea. Lobectomy was performed because of the diffuse involvement of the lobe. The postoperative x ray examination revealed complete re-expansion of the left upper lobe without any evidence of emphysematous changes. The patient completed her training and is now symptom free.

(Case 4—J. D.), a 44 year old man was a cobbler. Admitted to the hospital on March 12, 1945 the patient complained of cough, productive of slight amount of thin, mucoid sputum. At times the sputum was blood streaked. Progressive dyspnea associated with occasional wheezing was also present. The patient stated that three months previous to admission he felt a subtle break in his right chest and he raised a large amount of sputum, colorless material. This patient was diagnosed elsewhere as tuberculous. X ray examination of the chest on March 12, 1945 revealed that in the left base there were present a few curved gracile linear shadows suggesting air-containing cavities. On the right side lung markings were absent above the second interspace anteriorly and the fifth rib posteriorly. The x ray report was as follows: Possible pneumothorax pocket but the fine lines which formed the lower border of the area were more suggestive of a large emphysematous bulla. Right and left diaphragm were low in position. At operation March 14, 1945 excision and repair were done. In the right upper lobe a huge emphysematous bleb was found almost replacing the entire lobe. There were also a few emphysematous lobulations in the middle lobe.

Microscopic Diagnosis—Microscopic diagnosis was fibrous tissue with neoplastic lining consistent with emphysematous bleb.

Comment—The x ray appearance of the bleb could have been easily mistaken for an apical pneumothorax. This patient was diagnosed and treated for tuberculosis. Postoperative x ray view showed complete re-expansion of the lung and as yet showed no evidence of progression of the emphysematous changes found during operation in the middle lobe. Patient at the present time is asymptomatic.

(Case 5—W. B.), a man aged 49 years, was a plumber. He was admitted to the hospital in August 1943 complaining of progressive dyspnea on exertion and marked wheezing on

BRUCELLOSIS OSTEOMYELITIS

REPORT OF TWO CASES IN WHICH SHAFTS OF THE LONG BONES WERE INVOLVED

GEORGE H. LOWE, JR. M.D. *

AND PAUL R. LIPSCOMB, M.D. † ROCHESTER, MINN.

SYSTEMIC brucellosis during the acute phase characteristically produces two outstanding symptoms namely fever of varying degree and generalized aching especially in the lumbar portion of the spinal column and in the long bones. Might it not be reasonable to suppose that an embolus of species of *Brucella* could multiply in these bones to produce osteomyelitis? A search of the literature reveals substantial support for such a supposition because there are numerous reports of brucellosis of the lumbar part of the spinal column and an occasional record of a similar infection in other bones.

Since there are several excellent reports which describe brucellosis osteomyelitis in the lumbar portion of the spinal column, only brief mention of this particular lesion need be made herein. The few reported cases in which brucellosis osteomyelitis has involved bones other than the spinal column will be considered in more detail. Steindler¹ mentioned the largest series of recorded cases of vertebral infection; he said that up to 1939 fifty seven cases had appeared in the literature. He also added four cases of his own in which all signs pointed to infection with some species of *Brucella*. In only one of these four cases was the causative organism produced by culture of material taken from the lesion since this single case was the only one in which the treatment was surgical permitting of access to the lesion.

Kulowski and Wulke² summarized this single case of Steindler which was the first instance of proved brucellosis osteomyelitis. Kulowski³ also reported two cases of formation of abscess among ten cases of brucellosis of the spinal column. Generally conservative treatment eventually yields fairly good results as demonstrated by Steindler and Phalen, Prickman and Krusen⁴ the latter of whom employed fever therapy with success for two of three patients.

Steindler¹ and Kulowski³ in their overlapping reports referred to several interesting cases of extraspinal osteomyelitis proved by culture to have a basis in brucellosis. One patient who had had osteomyelitis of the humerus for six years was cured by sanerization and establishment of drainage. In another case after severe infection the head and neck of a femur finally healed and the hip joint underwent complete ankylosis with no treatment other than establishment of drainage. Cases of brucellosis osteomyelitis involving the skull and ribs an ischium and the bones of a hand also have been reported by Steindler and others.

Porter⁵ reported an instance of Donoghue⁶ described head Ankylosis of

*Read at the meeting of the Clinical Orthopedic Society, Rochester, Minn. Oct. 11 and 12, 1946.

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2 Emphysematous blebs and bulla, under certain conditions, are definitely incapacitated because of progressive dyspnea

3 A simple, conservative type of surgical treatment, with excision of the involved area and preservation of normal lung tissue, is described

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W. B. Saunders Company

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the hip with complete healing occurred after the establishment of surgical drainage. Conservative treatment as employed by Gardner and associates⁴ produced cure of a patient who had periosteal abscesses of the tibia and swelling of the knees, of one rib, and later of the right forearm. The lesions were proved by means of the results of biopsy and culture, to be those of brucellosis. Mazini and Carman⁵ of Argentina reported an instance of proved brucellosis of the femur. Two years after biopsy, the lesion was found to have remained active and possibly to have extended to the right humerus. A unique instance of brucellosis osteomyelitis of an exostosis in the lower femur was reported by Horstmann.¹⁰ There are numerous references^{1, 2, 3, 11, 12} to polyarticular infections in which the epiphysis may have been involved.



FIG. 1.—(a) Left hip and femur of the patient in Case 1. (b) Cross-section of the right femoral neck, showing a large, dark, irregular area of osteomyelitis in the right parietal region of the femur.

REPORT OF CASES

CASE 1—A veterinarian 34 years old was first seen at the Mayo Clinic in 1937, complaining of pain in the left hip and a draining sinus situated high in the right thigh. In 1928, after he had removed a placenta from a cow at the birth of a calf, an infection had developed on his arm, and soon had involved a gland in the axilla. Results of a cutaneous test for the organisms of brucellosis several months later were positive. The arm and axilla healed within a few weeks with no treatment.

In December, 1939, a sudden pain developed in the left hip. This persisted for approximately one month before it completely subsided. There was no fever during this period. A red, tender area appeared on the outer aspect of the right thigh in March, 1940, and was followed by a month of "flu." The red area was lanced in June and had drained since that time.

Two months prior to the patient's admission pain gradually developed in the left hip. It was aggravated by activity or pressure over the area. The patient lost fifteen pounds (6.8 kg) in the two months prior to admission.

Results of physical examination were essentially negative, except for discovery of a draining sinus situated in the upper part of the right thigh and the testimony of pain at pressure over the left greater trochanter. The patient was not febrile and had not been during the preceding months. Results of a blood count were essentially normal: leucocytes amounted to 9,100 per cubic millimeter, the differential count disclosed that 70 per cent of the leucocytes were neutrophils, 23 per cent were lymphocytes, 4 per cent were mononuclear leucocytes, 2 per cent were eosinophiles and 1 per cent were basophiles. Results of urinalysis and of flocculation tests of the serum were negative. Roentgenologic examination revealed a normal thorax and osteomyelitis of the right femur with cystic areas of the right femoral neck and of the left acetabulum and ileum.

On June 27, 1932, an abscess in the patient's right thigh was drained. A drill hole into the right femoral neck yielded a small amount of thick, yellow pus. It was felt that most of the symptoms over the left trochanter were based on bursitis.

About one year later an abscess posterior to the left greater trochanter was drained, and osteomyelitis in the right parietal region of the skull was detected by roentgen rays (Fig 1, *a* and *b*). Results of agglutination tests for brucellosis on two occasions during this visit were positive in dilutions of 1:80, and material obtained from the abscess produced the organisms of brucellosis when it was cultured. There were no symptoms referable to the right hip but the hip sinus continued to drain. The wound in the left hip healed rapidly.

In 1933 a roentgenogram revealed marked thickening of the cortex at the inner aspect of the upper part of the right femur, along with an old area of cystic destruction situated below the trochanter and in the femoral neck.

Despite the administration of vaccine and frequent courses of therapy with sulfonamide compounds, the lesions remained active. In a letter from the patient received in 1940 he reported that he had been in bed most of the previous year.

CASE 2—A farmer 45 years old entered a hospital in November, 1945 complaining of fever and a swollen, painful red area over the medial aspect of the lower part of the left thigh.

For one

temperature was as high as 102° F (38.3° C) and lost fifty four pounds (24.5 kg) in the last six months. This had occurred in cattle

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Although he had had no specific complaint, or since the fever. Detailed questioning re of the left thigh for seven years, but that he only when pressure was exerted over the area. Five weeks prior to admission, severe pain had developed in the lower and anterior part of the left thigh. Shortly thereafter temperature had increased to 103° F (39.4° C). Both fever and pain had continued.

Physical examination revealed a poorly nourished, flushed, febrile man who had a tremendously swollen, red area over the lower part of the left thigh. Other observations disclosed nothing abnormal except for a temperature of 100° F (37.8° C). Studies of the blood revealed that the result of a flocculation test of the serum was negative, that the value for hemoglobin was 13.4 Gm per 100 cc of blood, that erythrocytes numbered 4,370,000, and that leucocytes numbered 14,700 per cubic millimeter of blood. Results of two agglutination tests were positive for the organisms of brucellosis in dilutions of 1:80. Marked osteomyelitis with sequestration in the lower part of the left femur was demonstrated in roentgenograms (Fig 2, *a* and *b*).

Penicillin was administered for several days prior to performance of sequestrectomy. A large abscess, connected through a small cloaca with the region involved by osteomyelitis, was found in the anterior medial portion of the thigh. The pus from the abscess was thick and brown, and the bone marrow well along the femur had been replaced by a very thick cheese-like yellow, highly odiferous material. A sequestration and a sequestrectomy operation

were performed. The wound was packed open with petrolatum gauze, and the knee held at rest with a Thomas splint. The patient began to carry out graduated knee exercises several days after the operation.

Microscopic studies of tissue removed at the time of surgery revealed subacute and chronic osteomyelitis with peculiar zones of caseous-like necrosis, and the pathologist noted that this was possibly on the basis of *Brucella* infection. Results of both culture and examination of smears were positive for the organisms of brucellosis.

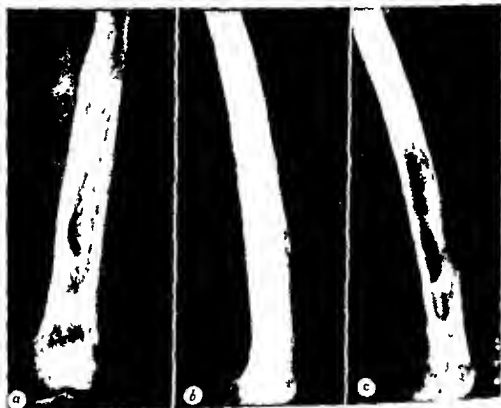


Fig. 2. The lower part of the humerus.

After operation the patient received two courses of 240,000 units of streptomycin daily. The first course lasted for two weeks; the second was completed in one week with a ten-day rest period between the two. Pain and fever disappeared immediately after the operation. No conclusion was drawn concerning the value of the streptomycin employed.

After the operation the amount of material drained gradually decreased and the bone appeared to be healing slowly. The patient was seen in June 1946 (Fig. 2 c) at which time moderate drainage was still present.

Small quantities of purulent discharge persisted until March 25 1947 at which time the scar was excised and the sinus curetted thoroughly revealing healthy bleeding bone. No brucellosis organisms were found after culture of the excised tract. Multiple small pieces of bone from the left humerus were placed in the bony defect. A plastic prosthesis was performed. There has been no sign of recurrence.

COMMENT

The diagnosis of brucellosis of the shafts of long bones should not be difficult to make if the possibility of presence of the condition is constantly borne in mind. In nearly all instances a history of relatively recent and obscure fever, with pain in bones and the lumbar part of the spinal column, will be obtained. However since uncomplicated brucellosis osteomyelitis generally is of low virulence it may be difficult in many cases to obtain a history of recent infection. Chronic osteomyelitis not accompanied by drainage and producing little discomfort and disability should be suspected of having a basis in brucellosis. Agglutination tests are of little value unless the results are strongly positive since in most cases in which the disease is long standing the titer is within the upper limits of normal. Frequently the pus is cheesy and grossly different from that associated with the usual pyogenic infection. Careful microscopic study will reveal a giant cell type of reaction with irregular caseation which may be confused with that of tuberculosis. When there is any suggestion of the presence of the aforementioned variations from the typical manifestations of classic osteomyelitis material from the lesions should be carefully cultured. If the foregoing suggestions are carried out many more instances of brucellosis of the bones should be detected than have been found in the past.

Probably a saucerization operation preceded and followed by the use of penicillin in an attempt to prevent secondary infection will yield the best results in brucellosis osteomyelitis other than that of the spinal column. When brucellosis osteomyelitis of the spinal column is present, conservative treatment should be in order, unless actual formation of abscess has occurred. The value of streptomycin in the treatment of brucellosis osteomyelitis remains to be evaluated.

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CIRCULATORY CHANGES PRODUCED BY CLAMPING OF THE THORACIC AORTA

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SURGICAL excision of the anomalous segment of aorta for treatment of congenital coarctation of that vessel was reported in 1945 by Crafoord and Nylin¹ and Gross and Hufnagel.² Clamps were applied to the aorta above and below the usual site of coarctation at the *ligamentum arteriosum*. The proximal clamp was applied just distal to the left subclavian artery so that circulation to the head and upper extremities was unimpaired. Blood flow distal to the clamps was maintained through collateral channels around the obstruction. After the constricted segment of aorta had been excised continuity of the vessel was re-established by end-to-end anastomosis. In the first human being operated upon by Gross immediately after the clamps were released, the heart went into uncontrollable dilatation and the patient died.^{2,3,4} Gross thought that the failure was caused by inadequate return of blood to the heart after the clamps were released. In his subsequent operations the clamps were released slowly over a period of minutes with the patient in the Trendelenburg position. The rate of blood infusion was increased during the period of unclamping. After these precautions were adopted no further deaths were reported. Concerning the cause of heart failure, Gross said.⁴ "From some of our experimental work and from a disastrous outcome in one case it is evident that a quick removal of the last aortic clamp may impose a momentary but serious burden on the cardio-vascular apparatus. The sudden opening up of an enormous vascular bed in the lower part of the body makes great demands upon the heart. The cause of death in the first patient has been loosely described as cardiac collapse since the exact mechanism of failure is not known. Presumably, it was a form of 'shock' because blood flowed rapidly into the depleted system in the lower two thirds of the body, pooled there and did not return quickly enough to supply the heart with a circulating medium."

Crafoord had not observed such cardiac failure despite experience with the aortic occlusion maneuver both during excision of coarctation and during division of patent ductus arteriosus. In view of the added strain imposed upon the heart by such obstruction and the abnormal conditions which must prevail immediately after release of the clamps the following experiments were carried out in an effort to determine whether the failure could be explained by existing concepts or whether factors hitherto undescribed played a part.

EXPERIMENTAL

Methods—Ten mongrel dogs of varying age and sex were used. The weight of the animals varied from seven to fifteen kilograms. Nine of the ani

imals were anesthetized with nembutal given intravenously in doses of 30 mg per kilogram of body weight. One of the animals was anesthetized with cyclopropane and oxygen in a closed circuit with a soda lime canister. The trachea was cannulated in each animal. In animals anesthetized with nembutal, during the period when the chest was opened widely, respiratory exchange was maintained by intermittent blasts of compressed air delivered by a mechanical respirator. In the animal anesthetized with cyclopropane, respiratory exchange was maintained by rhythmical pressure on the breathing bag of the anesthetic machine. No preoperative medication was given to the animals anesthetized with nembutal. The dog treated with cyclopropane received 30 mg of morphine sulfate by subcutaneous injection during the immediate preoperative period.

The animal was placed in the dorsal decubitus on an animal board which was horizontal in all but one of the experiments. The trachea was cannulated in the neck. The internal mammary arteries were drawn up into the neck incision with an aneurysm hook, and ligated. The anterior part of the chest wall was then removed by incision at the costochondral junctions with minimal loss of blood. The end arterial pressure in the left carotid artery and left femoral artery was measured by mercury manometer. A 15 gauge hypodermic needle was inserted into the superior vena cava a few millimeters above the atrium. The needle was directed toward the heart. The needle was connected to a small bore manometer containing 0.5 per cent heparin in physiologic saline solution. Venous pressure readings were taken visually and the time of reading was indicated by a mark on the kymograph drum. Care was taken that the needle did not come in contact with the sinus area. In some of the animals volume changes in the leg and in a segment of small intestine were measured by plethysmograph connected to a recording water manometer. The thoracic aorta was mobilized distal to the origin of the left subclavian artery and obstructed in continuity with a clamp similar to the one described by Gross and Hufnagel.² Care was taken during the application of this clamp that it did not press upon the vagus nerve or left pulmonary artery. During one experiment arterial blood samples were analyzed for pH with the glass electrode and for lactic acid by the colorimetric method of Barker and Summerson.⁶

Results—Immediately after clamping the aorta there was a rise of carotid arterial pressure, the increment amounting to 40 to 60 mm of mercury. The response illustrated in Fig. 1 is typical except that in most of the records the rise of arterial pressure was prompt and sustained. Femoral pressure fell rapidly. Although all pulsations were eliminated from the femoral artery tracing, the pressure did not fall to zero but stabilized at around 20 mm of mercury. There was a pronounced slowing of pulse rate which was probably due to the rise of arterial pressure in the carotid and aortic reflexogenic areas. The slowing was less pronounced under nembutal anesthesia than under cyclopropane anesthesia. During this period the heart visibly increased in size and contractions seemed more vigorous.

In all experiments there was a rise of venous pressure after application of the clamp. The rise varied from 5 to 50 mm of saline solution. The rate of

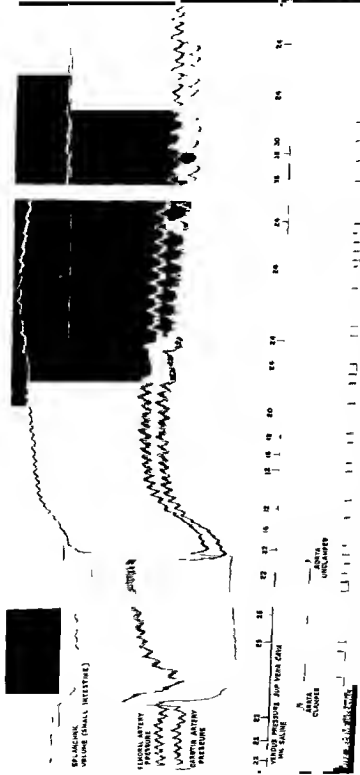


Fig. 1.—Response to reperfusion and unclamping of the aorta in a dog under nembutal anesthesia. The first break in the record represents an interval of 5 minutes. The second break represents an interval of 30 minutes.

rise was variable occasionally rising promptly to a plateau and occasionally showing progressive elevation throughout the entire period of obstruction. Uniformly there was a fall in the volume of enclosed small intestine. The fall of volume continued throughout the period of clamping. Leg volume recording showed little change (probably due to lack of sensitivity in our apparatus). One or two of the records showed slight reduction in the volume of the leg following application of the clamp but such a change was so slight that adequate evaluation could not be made.

The aorta was obstructed for varying lengths of time ranging from five to fifteen minutes. Although resection of a segment of aorta and end to end anastomosis require from twenty to sixty minutes it was felt that similar circulatory changes could be elicited by shorter periods of clamping. In two of the records the carotid arterial pressure showed a tendency to rise gradually over a period of minutes after the sharp initial rise. This was not a constant finding. In one record frequent extrasystoles were noted. This was the only time in regular heart rhythm was noted. The extrasystoles disappeared after the clamp was released and a normal response to removal of the clamp was seen.

During all but one of the experiments the aortic clamp was released suddenly so that maximal effects would be produced. Immediately after release of the clamp there was a fall in the carotid arterial pressure to a level far below that existing before the clamp was applied. The fall was precipitous and was completed in a period of a few seconds. During that time the femoral arterial pressure rose to its normal relative position above the carotid arterial pressure. There was then a compensatory period during which the arterial pressure rose before finally falling to a stable level. Stabilization occurred within 90 to 180 seconds after release of the clamp. The blood pressure was usually lower during the stable period than the pressure before the clamp was applied.

There was a pronounced increase in the volume of the enclosed small intestinal segment above the volume existing before the clamp was applied. In the face of lowered arterial pressure this finding is indicative of splanchnic vasodilatation. Stasis of blood in areas distal to the clamp was demonstrated in one experiment by a rise of plasma lactic acid concentration and fall of plasma pH. Such an accumulation of metabolites is known to produce vasodilatation of small vessels. In these experiments the vasodilatation was not demonstrated by increased organ volume until after the arterial pressure in the visceral blood vessels was elevated by release of the clamp. There was then pooling of blood in the dilated vessels and an increase of organ volume. Such an effect is comparable to the reactive hyperemia seen in an extremity after removal of a tourniquet which has obstructed the blood supply for a period of time. The pooling of blood was accompanied uniformly by a fall of venous pressure in the superior vena cava indicating inadequate return of blood to the heart. Compensatory mechanisms had returned the venous pressure to adequate levels before the maximal splanchnic dilatation was seen in Fig 1. The gradual return of splanchnic volume to preclamping levels was accompanied by a sustained rise of venous pressure above levels noted before the clamping.

Despite the fact that the aorta was clamped and unclamped two or three times in each animal none of the animals expired during the period of stabilization after release of the clamp. One of the animals died about five minutes after the clamp was released and after arterial pressure and pulse rate had apparently stabilized. The changes in this animal are illustrated in Fig 2. There was a progressive fall of venous pressure after release of the clamp. The low arterial pressure and rapid pulse indicated that the animal was in poor condition. The fall of venous pressure was not accompanied by accelerated pulse rate or fall of blood pressure during the time when the kymograph drum was running, such effects were observed for only a short period of time after the drum was stopped.

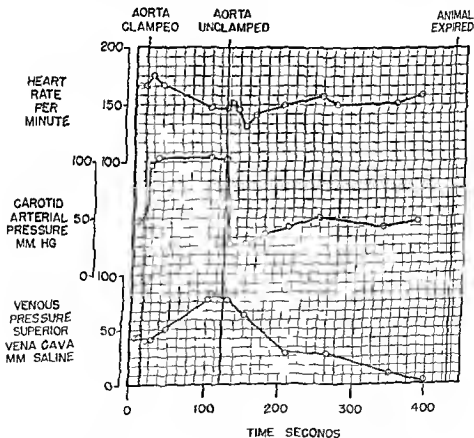


Fig 2.—Circulatory changes prior to death in an animal under nembutal anesthesia showing the progressive fall of venous pressure in the superior vena cava.

In each of the animals, after release of the clamp there was an increase in pulse rate. Again the alteration was less pronounced under nembutal anesthesia than under cyclopropane anesthesia. Typical effects of the two anesthetic agents are illustrated in Figs 3 and 4. When nembutal was used the pressure

fell to lower levels during performance of the preliminary operations. This is attributed to the depressing effect of barbiturates on blood pressure associated with the trauma of removing the anterior chest wall. When the clamp was applied, the elevation of blood pressure was as prompt and as great with cyclopropane, as with nembutal. In the animal treated with cyclopropane, there was a sharply reduced pulse rate, an expected response to elevated blood pressure. In the animal anesthetized with nembutal the pulse rate in this instance was actually accelerated for about one minute after application of the clamp.

NEMBUTAL ANESTHESIA

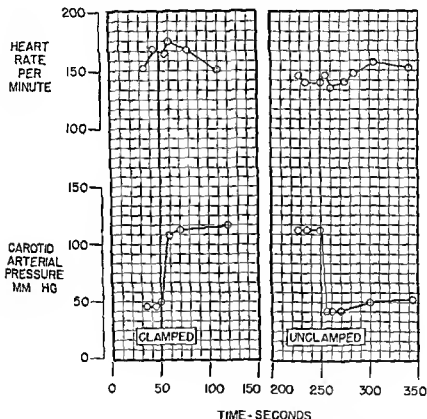


Fig. 2.—Response of arterial pressure and heart rate to clamping under nembutal anesthesia. Note the sluggish response of pulse rate to rapid fluctuations of arterial pressure.

There was then a gradual fall of heart rate during the remainder of the period of clamping. The bradycardia never assumed the proportions noted in the animal anesthetized with cyclopropane. Although the aorta was obstructed for a shorter period of time in the animal treated with nembutal, it was occluded for a length of time manyfold that during which maximal bradycardia was produced in the animal anesthetized with cyclopropane. Release of the clamp elicited a prompt fall of arterial pressure in both animals. The pulse rate under

cyclopropane rose from 104 to 192 in two minutes. The pulse of the animal treated with nembutal was only slightly accelerated. This may in part account for the stabilization of arterial pressure at a low level in the animal under nembutal at a time when the arterial pressure in the animal under cyclopropane was still rising. The usual anesthetic agents used in clinical thoracic procedures should elicit a response in pulse rate similar to that produced by cyclopropane.

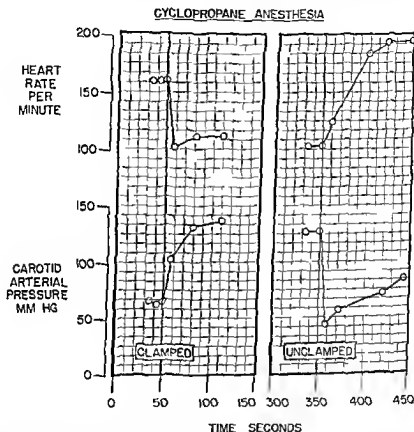


Fig 4.—Response of arterial pressure and heart rate to clamping under cyclopropane anesthesia. Note the prompt response of heart rate to rapid fluctuations of arterial pressure.

In one experiment blood samples were withdrawn from the ascending aorta near the coronary ostia and analyzed for lactic acid and pH. The clamp was released after only eight minutes obstruction. There was then a progressive rise of arterial lactic acid concentration over a period of three minutes after unclamping rising to a maximum of 150 mg of lactic acid per 100 cc of plasma. Plasma pH fell during this period to a minimum of 7.2. Rapid buffering mechanisms were undoubtedly impaired by the mechanical regulation of gas exchange.

DISCUSSION

A pronounced increase of splanchnic volume is seen after the clamp is released despite the lowered arterial pressure. This would indicate appearance of reactive hyperemia in tissues distal to the site of aortic occlusion and consequent pooling of blood in dilated vessels. The pooling of blood was accompanied by a reduction of venous return to the heart as indicated by a fall of pressure in the superior vena cava. The fall of venous pressure would suggest that the mechanism of failure is based upon inadequate filling of the heart chambers that is a hypodiastolic failure. Such a train of events was considered by Gross to follow release of the clamp. He introduced certain measures to insure that cardiac failure would not occur. The protection afforded by two of Gross' maneuvers, Trendelenburg position and slow release of the clamp, is illustrated in Fig. 5. Before the kymograph was started the animal was placed in the Trendelenburg position by elevation of the foot of the animal board eighteen inches. Throughout the record venous pressure was elevated. Although the typical rise and fall of venous pressure was seen, adequate venous return to the heart was maintained at all times. Release of the aortic obstruction over a period of forty-five seconds produced a gradual reduction of the carotid arterial pressure without the precipitous fall and compensatory rise seen when the clamp was released suddenly. Gross released the clamps even more slowly over a period of minutes. The splanchnic volume showed no increase above preclamping levels but gradually returned to approximately the preclamping level over a period of five minutes. Such an effect is probably due to a washing out of metabolites and improved oxygenation of anoxic areas with subsequent improvement of vasomotor tonus before the full force of arterial pressure is transmitted into the splanchnic vascular bed.

It is uncertain whether the acceleration of pulse noted in the animal treated with cyclopropane is a desirable adjustment to the fall of arterial pressure. The demand for increased cardiac output cannot be met by acceleration of pulse rate unless venous return is maintained at the same time. In the face of falling venous pressure cardiac acceleration can conceivably result in less economical utilization of energy by heart muscle due to the reduction of stroke volume.

In certain respects the conditions of these experiments differ from those prevailing in the human patient with coarctation of the aorta. Long-standing coarctation of the aorta is associated with the development of extensive collateral circulation around the site of constriction. Consequently there is less derangement of circulation distal to the clamps when a coarctation is isolated than when a normal aorta is clamped. That the circulation is not adequate in normal dogs is shown by the high incidence of hind limb paralysis noted by Gross and Hufnagel after they had divided and re-anastomosed the aorta. Deficiency of collateral circulation is further enhanced in the present experiments by ligation of the internal mammary arteries and upper intercostal arteries. Because of these conditions it is unlikely that changes as great as these would occur in the human patient, but it might be suspected that changes of a similar nature would be observed.

cyclopropane rose from 104 to 192 in two minutes. The pulse of the animal treated with nembutal was only slightly accelerated. This may in part account for the stabilization of arterial pressure at a low level in the animal under nembutal at a time when the arterial pressure in the animal under cyclopropane was still rising. The usual anesthetic agents used in clinical thoracic procedures should elicit a response in pulse rate similar to that produced by cyclopropane.

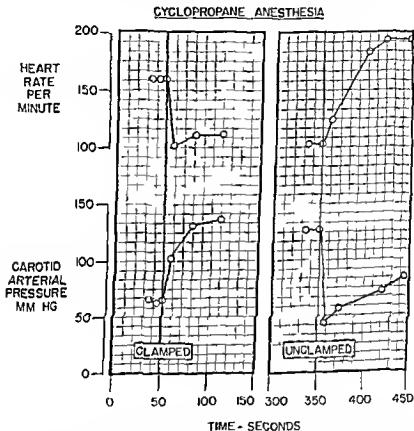


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Because of the mobile mediastinum the opening of one pleural space creates a bilateral open pneumothorax in the dog. Respiratory exchange must then be maintained by some device for insufflation of air or oxygen under positive pressure into the lungs. Similar conditions would prevail in the human being only where a bilateral open pneumothorax was created inadvertently by the surgeon or where a "controlled" type of bag breathing was instituted by the anesthetist. Under these conditions rapid variations in carbon dioxide content or pH would not be as rapidly compensated by altered ventilation since the patient would be separated from the control of his respiratory center.

SUMMARY

1 The thoracic aorta was obstructed in a series of dogs and the circulatory changes were studied by recording of carotid arterial pressure, femoral arterial pressure, pressure in the superior vena cava, splanchnic volume (small intestine), and leg volume.

2 Following obstruction of the thoracic aorta there is a rise in the pressure in the carotid artery and in the vena cava. After the clamp is removed there is a fall of carotid arterial pressure and a fall of caval pressure accompanied by a pronounced increase of splanchnic volume. The increased organ volume is attributed to pooling of blood due to vasodilatation in anoxic tissues distal to the site of aortic obstruction. The fall of venous pressure indicates inadequate return of blood to the heart.

3 Despite the conditions in these experiments which would be expected to impose a maximal strain upon the heart, death occurred only once immediately after the clamp was released. The death was preceded by a gradual progressive fall of venous pressure.

4 These findings support the suggestions of Gross that the heart failure he had observed in a human patient after surgical excision of a coarcted segment of aorta was caused by inadequate venous return to the heart. The supportive measures he introduced for assuring that venous return is maintained are shown to be well suited for that purpose.

I wish to thank Dr. William B. Youmans and Dr. William S. Cooklin for many helpful suggestions during the development of this paper.

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Fig. 5. Record showing the effect of the aortic clamp on the pressure in the superior vena cava and the cardiac output. The first 10 minutes of the record are taken with the aortic clamp in place. The second 10 minutes are taken with the aortic clamp removed.

guinal rings In addition, the patients were instructed to cough while the examining finger attempted to elicit a hernial cough impulse at the external ring Men in whom hernias were discovered during this examination were thereupon omitted from further consideration in this series

In thirteen men various difficulties were encountered which were serious enough to warrant rejection of the findings In ten of these men adequate examination was prevented by lack of cooperation or the tickling reflex, or both, while in three cases the subcutaneous rings could not be satisfactorily located by palpation despite adequate cooperation

A total of 221 men were excluded from this series for the reasons shown in Table I

TABLE I

	122
	66
	19
	10
Subcutaneous rings not satisfactorily located	3
Strapped wound of the inguinal region requiring extensive reparative surgery	1
Total	221

The terms "subcutaneous inguinal ring" and "external ring," are used synonymously in this report, as are the terms "abdominal inguinal ring" and "internal ring "

OBSERVATIONS

Of the 5 956 subcutaneous inguinal rings in the 2,978 men remaining after rejection of those listed in Table I, 78 1 per cent were large enough to admit the index finger without force The detailed findings are summarized in Table II

TABLE II. DISTRIBUTION OF THE SIZES OF 5,956 SUBCUTANEOUS INGUINAL RINGS FOUND IN 2 978 HEALTHY YOUNG MEN

Symmetrical

Of the sixty unilateral inguinal hernias discovered in this study, thirty five or 58 3 per cent occurred on the right side This tendency of hernias to occur on the right side has long been recognized It is usually attributed to the fact that the right testis descends later in the human fetus than does the left

On the other hand 57 5 per cent of the 724 men who had inguinal rings of unequal size had the larger ring on the left side The reason for this situation is not clear Perhaps the more frequent occurrence of varicocele on the left may offer a partial explanation

THE SUBCUTANEOUS INGUINAL RING A CLINICAL STUDY

JAMES ON L. CHASIN, M.D.,* MASPETH N. Y.

(From the Regional Hospital, Fort Jay, Governors Island 4, New York, and the War Department Separation Center Fort Monmouth New Jersey)

ROUTINE physical examination at an army separation center has served to emphasize certain points of confusion regarding examination of the inguinal region. Numerous textbooks^{1,2} state that the normal subcutaneous ring should not admit the tip of the index finger. Nevertheless, on routine palpation many apparently healthy young men were found to have large subcutaneous rings. Considerable disagreement arose as to the significance of this finding. There was no clear cut conception of the range of normal variation in the size of the external rings. Survey of the recent literature did not provide a solution to this problem. As a result this study was undertaken in order to determine the range of sizes of the subcutaneous rings in large numbers of healthy young men.

MATERIAL AND METHODS

Three thousand one hundred ninety nine (3,199) soldiers between the ages of 18 and 36 years, who were being separated from the service, formed the basis of this study. I examined these men for hernia as part of the final type physical examination. After considerable preliminary study the following examining routine, similar to that described by Carp³ was developed.

The patient stripped, stood erect before the examiner. Routine palpation of the scrotal contents was performed. The right index finger was used to invaginate the scrotum until the volar surface of the finger tip rode over the patient's left pubic tubercle. The finger then slid laterally for about 0.5 to 1.5 cm. at which point it suddenly dipped into a sharply delineated aperture comprising the subcutaneous inguinal ring. The identity of this structure was always confirmed by following the course of the spermatic cord into the inguinal canal.

Patency of the ring was tested by an attempt to insert the finger into the inguinal canal. Since cases have been reported⁴ of hernias which were traumatically induced by such a procedure it was carried out with some caution. The margins of the ring were explored with the finger tip and the length of the longest diameter was recorded. The width of my finger tip measuring 1.3 cm., served as a standard for estimating the diameter of each ring.

Following this step the patient was told to "strain down as if you were trying to move your bowels!" This action properly executed served effectively to increase intra abdominal tension and to force occult hernias through the in-

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*Formerly Captain Medical Corps Army of the United States Now at the New York Postgraduate Medical School and Hospital

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A total of 221 men were excluded from this series for the reasons shown in Table I

TABLE I

Preoperative	122
Cooperation	66
Cooperation	19
Cooperation	10
Cooperation	3
Extensive	1
Reparative surgery	1
Total	221

The terms 'subcutaneous inguinal ring' and 'external ring,' are used synonymously in this report as are the terms 'abdominal inguinal ring' and 'internal ring'

OBSERVATIONS

Of the 5 956 subcutaneous inguinal rings in the 2 978 men remaining after rejection of those listed in Table I, 78.1 per cent were large enough to admit the index finger without force The detailed findings are summarized in Table II

TABLE II DISTRIBUTION OF THE SIZES OF 5 956 SUBCUTANEOUS INGUINAL RINGS FOUND IN 2 978 HEALTHY YOUNG MEN

DIAMETER OF	
0.9	
Symmetrical	506
Asymmetrical*	163
Total	669
Per cent distribution	11.2%

*Of the 724 men in this group the left side

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On the other hand 57.5 per cent of the 724 men who had inguinal rings of unequal size had the larger ring on the left side The reason for this situation is not clear Perhaps the more frequent occurrence of varicocele on the left may offer a partial explanation

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is congenital patency of the processus vaginalis^{17 18} and the most important line of defense is a competent internal ring¹⁹. Once an incomplete hernia has entered the inguinal canal it is unlikely that a small subcutaneous ring can do more than delay the eventual descent of a complete indirect hernia.

Further evidence regarding the significance of a large external ring can be adduced from the follow up studies of Colecord and of Gardner. Colecord²⁰ found enlarged or 'open' external rings in 784 out of 9 000 men whose physical condition was checked frequently during their periods of employment. The incidence of hernias in the group of men with open rings was not significantly greater than in the control group. Gardner²¹ found that 3 413 (or 13.6 per cent) of a group of 24 934 civil service pre-employment physical examinations revealed relaxation of the external rings. In the subsequent fifteen year period ten men who had had relaxed rings (an incidence of 0.322 per cent) and forty-two men of the control group (0.176 per cent) developed hernias. Although this difference in incidence rates may appear to be statistically significant it is certainly not unpressive. Much more striking is the fact that of 3 413 men with relaxed rings who were admitted to full industrial employment in a navy yard only ten were known to have developed hernias over a period of fifteen years.

Considering these facts it would seem reasonable to conclude that there is at this time no convincing evidence that a large subcutaneous ring either is in itself an abnormal finding or that it predisposes to the future development of herniation. Nor should it be thought to disqualify men from industrial employment.

An attempt was made during this study to correlate the size of the subcutaneous rings with the height and with the weight of the patient but no correlation could be demonstrated. No attempt was made at correlation with the length of the inguinal ligament although this might prove interesting in view of the work of Harris and White²² and Hullenbrand²³ which indicates that men with long inguinal ligaments are more likely to develop weakness and herniation of the direct type than are men with short inguinal ligaments.

SUMMARY AND CONCLUSIONS

- 1 In a series of 2 978 healthy young men 78.1 per cent of the subcutaneous inguinal rings were large enough to admit the examiner's index finger.
- 2 Of the 724 men whose subcutaneous rings were not bilaterally equal in size 57.5 per cent were larger on the left side.
- 3 Enlargement of the subcutaneous ring alone should not be considered to be abnormal nor is there any conclusive evidence that it constitutes a predisposing factor in the pathogenesis of inguinal hernia.
- 4 There was no correlation between the size of the subcutaneous ring and either height or weight.

The author wishes to express his appreciation for the advice and criticism of Dr Henry A. Haskins, Baltimore, Md. and Dr Charles G. Mixer, Boston, Mass.

DISCUSSION

*Gray's Anatomy*⁹ gives the measurements of the subcutaneous ring in cadavers as 2.5 by 1.25 cm. However, according to various authorities, the dimensions of this structure, as determined by clinical examination, are as follows:

"It (the annulus inguinalis subcutaneus) should merely admit the tip of the little finger, if more than this is possible, the ring is not of normal dimensions" (Jason,¹ p. 377)

"The normal external ring will seldom admit the tip of the little finger and it is impossible to palpate the inguinal canal or the internal ring" (Watson,² p. 118)

"Ordinarily this (external abdominal) ring will not admit the finger tip, although about 3% of male adults have a larger or relaxed ring which predisposes to the later occurrence of direct herniae" (Erdman in Christopher,³ p. 1369)

"Normally it is barely large enough to admit the tip of the index finger" (Cole and Elman,⁴ p. 766)

"In a healthy man the external ring should admit the tip of the little finger but not the index finger. If the end of the index finger can be entered into the ring that aperture is dilated and even if there is no hernia in the canal in the future a hernia will probably descend" (DaCosta,⁵ p. 1050)

"The ring when normal in size cannot be entered by the tip of the index finger" (Callander,⁶ p. 289)

"The average normal external abdominal ring will not completely admit the tip of the fifth finger" (Orr,⁷ p. 471)

Several other standard surgical reference books¹⁰⁻¹² do not give any measurements for the normal subcutaneous ring.

Our results (Table II) are not consistent with these quoted statements since 78.1 per cent of the healthy young men in this select series had subcutaneous rings large enough to admit the index finger. This would tend to show that the range of variation among normal external rings is rather wide. Also the average ring is probably significantly larger than was heretofore believed.

The question then arises as to whether a large subcutaneous ring may predispose to the future development of inguinal hernia, especially of the direct type. This is the contention of Erdman in Christopher³ and DaCosta⁵ as quoted previously. On the other hand considerable evidence has accumulated¹³⁻¹⁶ which points to weakness of the transversalis fascia as the major factor in the pathogenesis of direct hernia. In almost all of our cases the transversalis fascia forming the posterior wall of the inguinal canal in the region of Hesselbach's triangle was found to be tense and unyielding when the patient was subjected to the straining test. This was true even among the men who had subcutaneous rings 4.0 and 5.0 cm. in length.

In the case of indirect hernia it is even less likely that enlargement of the external ring is a predisposing factor. Here the essential etiological mechanism

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In the case of indirect hernia it is even less likely that enlargement of the external ring is a predisposing factor. Here the essential etiological mechanism

AMBULATORY TREATMENT OF HALLUX VALGUS

EDWARD L. COMFORT, M D, and WILLIAM J. SCHULTZ, M D, CHICAGO, ILL

(From the Department of Bone and Joint Surgery Northwestern University Medical School)

PROLONGED rigid splinting and restriction of walking activity for periods of from two to six weeks have constituted the routine of most orthopedic surgeons after operations for correction of hallux valgus. As a result of this prolonged immobilization without the functional stimulus of weight bearing and walking, some permanent loss of motion in the metatarsal phalangeal joint has followed many of the operations. Hallux rigidus or hallux varus, which occasionally resulted, produced severe disability.

In addition to these complications, which may be relatively infrequent in the hands of experienced orthopedic surgeons, there is always greater cost and hence an economic objection to prolonged hospitalization made necessary by the usual procedure of rigid splinting and non weight bearing for a period of several weeks.

During the years 1940 and 1941, one of us (E. L. C.) conducted an outpatient clinic in the Central Free Dispensary of Rush Medical College. The patients in this clinic were mostly adults and a considerable proportion of them were 45 years of age or older. A common complaint of patients coming to the clinic was that of painful feet due to bunions. It was impossible to obtain hospital beds for service patients of this type. We determined to attempt to carry out surgical procedures for excision of the bunions and correction of the hallux valgus in the operating room of this outpatient clinic.

The operations were carried out under local anesthesia. The block of the metatarsal phalangeal region was started at midfoot and a tourniquet applied around the foot at that level. The surgical techniques used included the McBride, the Mayo and the Silver operations with various modifications. The sesamoid bones were removed whenever they were found to be hypertrophied or their articular surfaces degenerated. Debridement of the joint was carried out when indicated. No rigid splint of any kind was used. *In each instance the toe was held in a position of varus by corrective bandaging (Fig 1).* The blood which subsequently stained the dressing dried to further reinforce the bandage. Patients were permitted to walk from the operating room without assistance (Fig 2). Absence of pain because of the novocain anesthesia made it comparatively simple to persuade them to do this. Most of them had to go home by streetcar and some of them traveled long distances. The dressing was inspected the following week, but was not changed for two weeks after the operation.

A total of twenty four patients were subjected to one or more operations for hallux valgus and then permitted to go home immediately by whatever

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local or because other surgical procedures were to be carried out simultaneously. In eleven cases 1 per cent novocain was used as a local anesthetic. The patients who were operated upon under local anesthesia were encouraged to walk about their rooms immediately after the operation and were given bathroom privileges. Because of the persisting anesthesia they experienced no pain. On the second and third day these patients did complain of some pain but not sufficient to prevent them from bearing weight and walking.



Fig. 2.—Photograph following bandaging of great toe to demonstrate how well the toe may be held in a varus position without any type of rigid splint. Overcorrection by means of bandaging requires many layers of bandage, preferably two complete gauze bandages being used. This is the most significant departure from the standard treatment of bunions and makes possible immediate ambulation.

The patients for whom this procedure was used included a range of ages from 23 to 75 years. The occupations were those in which at least an average amount of walking was necessary. These patients were discharged as recovered four to eight weeks following surgery. There have been no complications or

transportation they could obtain. There were no complications. The results which were obtained were *definitely* better than those which had been observed in our patients whose care had included two to three weeks of hospitalization with complete immobilization. These patients suffered minimal pain and all of them returned to the clinic walking surprisingly well and with an excellent range of motion in the metatarsal phalangeal joint (Figs 3 and 4).



Fig 1—Artist's sketch of bandaged splinting male immediately after bilateral bunionectomies under local anesthesia with the patient standing.

One patient a chronic alcoholic disappeared after the operation and did not return for the postoperative appointments. When he was finally located more than a month after operation he still had the original dressing. Although the bandages were extremely dirty and ragged the wound was found to be completely healed. There was no swelling and the range of motion and strength in the movement of the hallux was approximately normal.

Encouraged by these results our program of care for private patients was changed to conform. Since 1941 we have performed twenty-six operations on seventeen hospitalized patients for hallux valgus and bunions. A general anesthetic was used in six cases because the patient refused to permit the use of

unfortunate sequelae and we are enthusiastic about this method of ambulatory treatment without rigid splinting

The plan of postoperative care may be summarized as follows

1 The hallux should be splinted by means of corrective bandaging without rigid fixation following operation Two two inch gince bandages should be used for each foot *Multiple layers of bandage* are essential if correction of the hallux valgus is to be maintained while ambulation is permitted

2 Walking with full weight bearing is begun immediately when a local anesthetic is used and on the day following an operation carried out under general anesthesia

3 The patient may be discharged from the hospital two to four days after operation

4 The original dressing should be changed and the stitches removed four teen days after operation

5 The functional splinting by corrective bandaging should be continued for an additional period of two weeks

6 Patients may be encouraged to resume their normal activities at the time that the bandaging is discontinued

7 After bandage splinting is discontinued the foot should be soaked in warm slightly soapy water for twenty minutes each day While in the warm water the toe should be actively exercised

8 Low heel soft leather oxford shoes with a stiff shank straight inside last and metatarsal pads should be worn for at least three months

The advantages of functional splinting without rigid fixation of the hallux after operation for the cure of hallux valgus include

1 Immediate activity with walking Hallux valgus is corrected while flexion and extension are permitted

2 Motion in the metatarsal phalangeal joint is preserved by early function

3 The hospital stay is greatly shortened

4 Circulatory changes in the foot which are common sequelae of prolonged immobilization and inactivity are minimal

5 Time lost from work is reduced



Fig 3—These preoperative x rays show the hallux valgus deformity and exostoses of the first metatarsal bones



Fig 4—Same case as Fig 3 following operation. Correction of the deformity is maintained by bandaging

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AN IMPROVED METHOD FOR PRODUCING EXPERIMENTAL PERITONITIS OF INTESTINAL ORIGIN IN DOGS

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EXPERIMENTAL peritonitis in dogs is not identical with peritonitis in human patients but it appears to be sufficiently comparable to serve as a useful medium for bacteriologic and physiologic studies and as an aid in the evaluation of therapeutic agents and methods.



Fig. 1.—Technique for producing experimental peritonitis of appendical origin. a Anatomical relations of the appendix often present in the dog. b Vascular supply of the appendix is ligated. c The base of the appendix is tied with a cotton tape. d The wall of the appendix is crushed uniformly with a clamp.

A procedure that consists of dividing the blood supply and ligating the base of the appendix followed by a dose of 54 cc. of castor oil has been described^{1, 2} as a suitable method of producing experimental peritonitis in the dog. However, following this procedure the appendix often becomes walled off by omentum and spleen and the infection remains localized without producing a peritonitis.

In an attempt to improve this method a series of dogs was subjected to the following procedure. The vascular supply of the appendix was divided and

This study was aided by a grant from the Christine Liron Fund
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ligated, a flat cotton tape $\frac{1}{4}$ inch in width was tied firmly about the base of the appendix the entire wall of the appendix was crushed by repeated clamping with a Kocher hemostatic clamp, the omentum was excised and the spleen removed, the animal was given 50 cc of castor oil by gavage. This procedure uniformly produced a fulminating diffuse peritonitis in all of a series of fifty six dogs. The average period of survival in untreated animals was thirty nine hours.

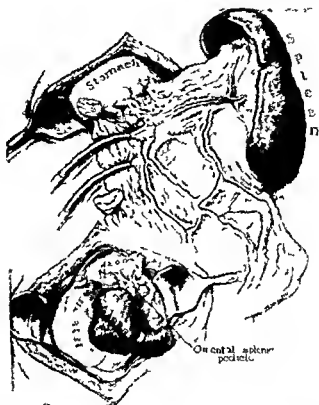


Fig. 2—Final step in technique for producing experimental peritonitis of appendiceal origin in dogs. Removal of omentum and spleen. Note crushed appendix with base ligated and vascular supply divided.

SUMMARY

A fatal fulminating diffuse peritonitis of appendiceal origin may be uniformly produced in dogs by a series of procedures including ligation of the appendiceal vessels, placing a tape ligature about the base of the appendix, crushing the wall of the appendix, excising the spleen and omentum, and administering castor oil postoperatively.

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EXPERIMENTAL PRODUCTION OF ULCERS IN CLOSED GASTRIC POUCHES IN DOGS

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A WEALTH of evidence attests the important role of acid pepsin in the production of experimental peptic ulceration and in the genesis of human gastroduodenal ulcerative disease. Although this evidence indicates that acid pepsin is a sine qua non for the existence of peptic ulcer, the cooperation of other factors is evident in both experimental and human peptic ulcers. For example, the continuous administration of histamine induces ulcers, but the relative importance of acid production and the antitoxic action of histamine in the genesis of these ulcers has not been elucidated.

One of the most important factors conditioning the effect of acid pepsin is the gradient of susceptibility manifested by the gastrointestinal mucosa. It is well known that the resistance of intestinal mucosa to gastric juice decreases progressively from the stomach to the colon. Exposure of the mucosa from the duodenum jejunum ileum or colon to relatively pure gastric juice usually results in ulcers. This may be accomplished by placing intestinal transplants in the stomach and preventing duodenal regurgitation, as in the method of Matthews and Dragstedt¹ by surgical duodenal drainage using the Mann-Williamson technique or by creating an experimental Meckel's diverticulum as in the experiments of Matthews and Dragstedt.¹ These procedures rarely result in gastric ulcers, and moreover the mucosa of isolated gastric pouches of most types, although in contact with pure gastric juice, seldom shows spontaneous ulceration. Dragstedt¹ reported the formation of ulcers in total gastric pouches in which vagus innervation was preserved. Ill² has not noted ulcers in total gastric pouches either with or without vagus innervation. In Dragstedt's experiments a metal cannula was used and this may have served as a mechanical to inhibit factor.

Ill, Vireo Code and Wengsten³ demonstrated that injections of histamine in beeswax produce duodenal and occasionally gastric ulcers in a large percentage of animals. These ulcers were attributed to the effect of prolonged maximal

These rather than

and caffeine cause in addition to stimulation of gastric secretion, vascular and inflammatory changes in the gastric mucosa.^{4,5} Therefore it must be considered questionable whether prolonged exposure of the gastric mucosa to acid pepsin is in itself sufficient to elicit ulcer formation.

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The following experiment was undertaken in an attempt to elucidate further the role acid pepsin plays in ulcer production and to ascertain if continuous exposure of gastric mucosa to normal gastric juice would result in ulcer formation

METHOD

Healthy mongrel dogs, weighing from 25 to 35 pounds, were used and all operations were performed under ether and morphine anesthesia with aseptic technique. A portion of the greater curvature of the stomach comprising one-third to one half of the fundus of the stomach, was resected in the first group of five dogs. This was done as in the Heidenhain technique,³ however, the resected segment was completely sutured into a closed pouch. Closure of both the stomach and the pouch was done by the open method using a separate continuous row of mucosal and serosal Lambert sutures.⁴ A clamp was used for the remaining gastric portion in all cases however in only three out of five was a clamp placed on the pouch.

A second group consisted of eight dogs. A two stage procedure was employed, the first being the construction of the usual Heidenhain pouch. After from nine to eighteen days, the dog was reoperated upon, and the stoma of the Heidenhain pouch was tightly sutured in two layers producing a closed gastric pouch.

A third group consisted of six dogs. Primary closure was established as in the first group, following which an avascular area of the middle or inferior end of the pouch was attached to the parietal peritoneum underlying the second left nipple, which was used as a point of localization. Twenty four hours post operatively a 15 gauge needle was inserted through the abdominal wall into the pouch a pressure determination was made with a water manometer, and gastric juice collected to relieve pressure and also for titration. Thereafter readings were made every twelve or twenty four hours depending on the volume collected and pressure within the pouch.

RESULTS

Group I (see Table I) —All five dogs in the first group died in two to five days due to acute ulcer formation with perforation and peritonitis. The site of ulceration was 0.6 cm from the suture line in three dogs, and 3 cm from the suture line in one dog.

TABLE I HEIDENHAIN POUCH TECHNIQUE PRIMARY CLOSURE

DOG NO	PROCEDURE	RESULTS
2	Heidenhain pouch closure without stoma	Died 2 days postoperatively, perforation of pouch with peritonitis
3	Heidenhain pouch closure without stoma	Died after 3 days, 1 cm ulcer of pouch with perforation 0.6 cm from suture line, peritonitis
4	Heidenhain pouch closure without stoma	Died after 5 days, 1 cm acute ulcer with perforation in central portion of pouch 3 cm from suture line, peritonitis
5	Heidenhain pouch closure without stoma, no clamps applied to pouch	Died after 3 days perforation of pouch 0.6 cm from suture line, peritonitis
6	Heidenhain pouch closure without stoma, no clamps applied to pouch	Died after 2 days perforation of pouch 0.6 cm from suture line peritonitis

Group II (see Table II) —Four of the eight dogs in the second group died of acute ulcers with peritonitis in three to eight days following closure of the stoma. Three dogs died of *intercurrent causes* without ulcer. One dog was sacrificed twenty days after closure of the stoma. The pouch was greatly distended, but showed no pathological change.

TABLE II HEDENHAIN POUCH, SECONDARY CLOSURE

DOG NO.	PROCEDURE				RESULTS
7	Hedenhain pouch	stoma	closed		Died 4 days after closure of stoma, leakage of stomal closure peritonitis
8	Hedenhain pouch	stoma	closed		Died 3 days after closure of stoma, pouch intact and filled with brown fluid several small mucosal erosions
9	Hedenhain pouch	stoma	closed		Sacrificed 20 days after closure of stoma evidence of much weight loss pouch intact greatly distended measuring 16 by 5 cm. mucosa thin and pale no erosions filled with thick milky fluid, black discoloration of omentum
10	Hedenhain pouch	stoma	closed		Died 13 days after closure of stoma, pouch
12	Hedenhain pouch	stoma			
				causes	
13	Hedenhain pouch	stoma			
16	Hedenhain pouch	stoma			
17	Hedenhain pouch	stoma	closed		near suture line Died 5 days after closure of stoma 0.8 cm perforation at superior end of pouch not near suture line abscess cavity extending from perforation filled with dark brown fluid and surrounded by omentum spleen and loops of small intestine

Group III (see Table III) —Four of six dogs in the third group died in seven to twelve days of acute ulceration of the pouch with perforation and acute peritonitis. Two of the dogs died in thirteen and fourteen days from extraneous causes. The average amount of gastric juice withdrawn for a twenty-four hour period the free acid range and average and the pressure range and average for each dog are noted in Table III.

All the animals with an average free acid concentration of over 40 meq per L. had acute ulcer formation with perforation. The two dogs which died of complications showed average free acid of 14 meq per L. and 36 meq per L.

DISCUSSION

The fate of closed gastric pouches has not been studied previously.

Perforation of the gastric pouch in Group I was questionably due to trauma caused either by the pressure of the clamp or by the underlying suture, for

TABLE III. HEIDENHAIN POUCH PRESSURE MEASURED BY ASPIRATION

DOG NO.	INCULCATE	FREE ACID CONCENTRATION		PRESSURE CM H ₂ O		AVF AMT WITH DRAIN PER 24 HR (CC)	PRE-ULCER	ULCER
		RANGE (NZ4 PER L)	AVE (BFQ PER L)	RANGE	AVE			
24	Closed Heidenhain pouch attached to abdominal wall for aspiration	1-51	59	10-50	29	89	Pressure 70 cc before every	ulcer 1 cm on pept of 5 mm crs sut ulcer ate gen na to 0.8 touch at site as puncture ate ulcer foration is, per ture base superior such an l
25	Closed Heidenhain pouch attached to abdominal wall for aspiration	44-117	70	0-63	24	149	Pressure 70 cc before every	
26	Closed Heidenhain pouch attached to abdominal wall for aspiration	0-105	49	0-8	7	101	Pressure with death 17	
29	Closed Heidenhain pouch attached to abdominal wall for aspiration	0-59	14	0-20	2	37	Aspirate not c	
30	Closed Heidenhain pouch attached to abdominal wall for aspiration	0-76	36	0-20	8	111	Aspirate every 12 hours did not eat with loss 5 days	Died after 14 days, pouch and stomach normal
31	Closed Heidenhain pouch attached to abdominal wall for aspiration	0-79	41	0-10	4	53	Aspirate every 12 hours 5th and 6th days, pressure 6 cm H ₂ O and 20 cc withdrawn 24 hr before death	Died after 8 days 1 to 2 mm perforation of pouch at superior end acute generalized peritonitis

Group II (see Table II) — Four of the eight dogs in the second group died of acute ulcers with peritonitis in three to eight days following closure of the stoma. Three dogs died of intercurrent causes without ulcer. One dog was sacrificed twenty days after closure of the stoma. The pouch was greatly distended, but showed no pathological change.

TABLE II HEIDENHAIN POUCH SECONDARY CLOSURE

DON NO	PROCEDURE			RESULTS
7	Heidenhain pouch	stoma closed	after 14 days	Died 4 days after closure of stoma leakage of stomal closure peritonitis
8	Heidenhain pouch	stoma closed	after 16 days	Died 3 days after closure of stoma pouch intact and filled with brown fluid several small
9	Heidenhain pouch	stoma	after 14 days	
10	Heidenhain pouch	stoma closed	after 18 days	omentum died 13 days after closure of stoma pouch
12	Heidenhain pouch	stoma	after 17 days	
13	Heidenhain pouch	stoma closed	after 17 days	cavity died 8 days after closure of stoma acute ulcer superior end of pouch 5 cm in diameter and 7 cm from suture line small perforation of ulcer with acute peritonitis free fluid in peritoneal cavity
14	Heidenhain pouch	stoma	after 9 days	died 10 days after closure of stoma chocolate
17	Heidenhain pouch	stoma closed	after 13 days	Died 8 days after closure of stoma ulcer perforation at superior end of pouch not near suture line abscess cavity extending from perforation filled with dark brown fluid and surrounded by omentum spleen and loops of small intestine

Group III (see Table III) — Four of six dogs in the third group died in seven to twelve days of acute necrosis of the pouch with perforation and acute peritonitis. Two of the dogs died in thirteen and fourteen days from extraneous causes. The average amount of gastric juice withdrawn for a twenty-four hour period, the free acid range and average and the pressure range and average for each dog are noted in Table III.

All the animals with an average free acid concentration of over 40 meq per L had acute ulcer formation with perforation. The two dogs which died of complications showed average free acid of 14 meq per L and 36 meq per L.

DISCUSSION

The fate of closed gastric pouches has not been studied previously.

Perforation of the gastric pouch in Group I was questionably due to trauma caused either by the pressure of the clamp or by the underlying suture for

SUMMARY

In Group I primary closure of the Heidenhain pouch in five dogs resulted in acute ulcer formation with perforation in all cases.

In Group II secondary closure of the Heidenhain pouch in eight dogs resulted in acute ulcers with perforation in four cases. Three died of extraneous causes and one that was sacrificed after twenty days showed no pathologic change.

In Group III primary closure of the Heidenhain pouch with daily aspiration of the pouch resulted in acute ulcer with perforation in four of six dogs. Two died of other causes without pathologic change of the pouch. All those in which the free acid averaged over 40 had ulcers of the pouch with perforation.

The method used in Group III may prove of value in the study of secretory pressure of the gastric glands.

CONCLUSIONS

In the majority of cases acute ulcers with perforation develop in closed Heidenhain gastric pouches. The relative importance of acid pepsin and high intraluminal pressure in the genesis of these ulcers is discussed.

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there was only one instance of perforation distant from the suture line. In an attempt to remove this factor the clamp was omitted in two cases. The results were not conclusive; thus a second group of operations was performed in which healing was complete in five sixths of the pouch before closure. In no case of secondary closure was the perforation near either the new or the old suture line, thus eliminating the question of surgical trauma as a possible cause of the ulcer formation and perforation.

Two etiologic factors remained to explain the cause of the ulcers. The first was the action of normal gastric juice in continuous contact with the gastric mucosa. The second was pressure within the pouch which would tend to interfere with venous return and possibly cause stasis of blood flow leading to ulceration.

It is possibly of significance that in one case (Dog 9) an ulcer did not occur after twenty days in spite of marked distention of the pouch. Unfortunately, the contents of this pouch escaped before a measurement of pressure or a determination of acidity could be made.

Sperling and Wangenstein⁸ subjected closed ileal loops in the dog to sustained increases of intraluminal pressure and showed that when a pressure of 40 cm. of water was employed the bowel showed necrotic areas after seventeen to twenty hours and was abnormally permeable and nonviable. Twenty to thirty centimeters of water produced similar changes but required a longer period of time.

Burget and his co-workers⁹ found that dogs with closed jejunal loops can be kept alive for long periods of time provided the pressure in the loops is kept down by aspiration of the fluid.

The studies in Group III reduce to a minimum the factor of increased pressure as a possible cause of perforation. The average pressure (which approximates average maximal pressure for each reading would be close to maximum for the preceding twelve to twenty-four hour period) was in all cases less than 30 cm. of water. As shown in Table III Dogs 26 and 31 had lower pressures but higher free acid values than Dogs 29 and 30. The former developed ulcers whereas the latter did not. Driver and co-workers¹⁰ have demonstrated that an increase of intraluminal pressure from 0 to 41 cm. of H₂O greatly enhanced the necrotogenic action of acid pepsin in the jejunum. Even with frequent aspiration some pressure developed in the closed pouches. That this low pressure may have been an essential factor in perforation is a possibility which cannot be excluded.

Insertion of the needle into the pouch introduced mechanical trauma as a possible cause of ulceration. However in all cases of ulcer formation in Group III the ulcer was in the superior end of the pouch and not near the puncture site at the peritoneal attachment. The area of mucosa which had been repeatedly punctured during aspirations presented no detectable change.

Clinically conditions approaching those encountered in a closed pouch are found in pyloric stenosis; the increased pressure and increased secretory activity¹¹ often present in this condition may predispose to extension or perforation of an ulcer.

above the wooden platform (The bolts fitted with large washers pass through the openings previously drilled 1 and 5 inches from the upper ends of the up rights) The lower basket is placed directly on the wooden platform between the uprights and is fixed in position by bolts which pass through the lowermost openings in the uprights. The stand now is complete and is ready to receive the bottles (Fig 1 B)

Discarded Vacoliter bottles (1000 cc) are used and will be found to fit into the baskets snugly. The bottles are connected as shown in Fig 2. The lower (water seal) bottle is securely wired or taped to its basket and remains in position permanently. The upper (catch) bottle is removable for purposes of emptying. Fig 3 shows the apparatus (old model) in use.

The setup described has the following advantages:

1. The base is sufficiently stable to prevent the apparatus from being accidentally overturned.

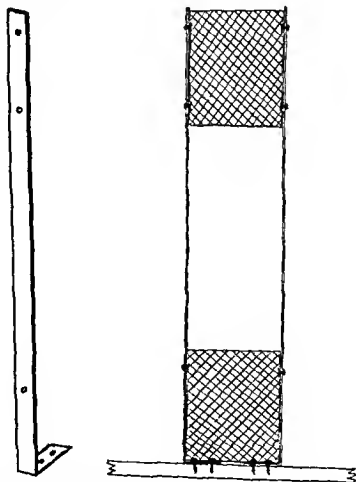


Fig 1—A Metal upright with drill holes in vertical and transverse arms. B Diagrammatic view of bottle stand. Metal uprights are fixed to wooden base by screws. Wire baskets are bolted to uprights through drill holes shown in A.

AN UNDERWATER DRAINAGE BOTTLE STAND

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EXPERIENCE has demonstrated that closed drainage of the thorax is maintained most effectively through the use of a water seal. The typical water seal closed system usually is comprised of two appropriately connected bottles, one (the catch bottle) serving to collect fluid which drains from the thorax and the other functioning as the water seal to prevent entry of air into the pleural cavity. Both bottles commonly are placed on the floor near the patient's bed where they constantly are in danger of being accidentally overturned or disconnected from one another or from the patient. Untrained personnel have a tendency to lift the bottles from the floor for inspection with the result that fluid may be aspirated from the seal bottle into the catch bottle and the water seal thereby broken.

While working in an Overseas Thoracic Center with a frequently changing and at times inadequately trained staff of ward attendants I devised a bottle stand which simplified the maintenance of an effective water seal to the point of making it practically foolproof. Once in operation the drainage apparatus required no attention other than to empty the catch bottle as required, and periodically to replace the small amount of water lost from the seal bottle by evaporation. The following are the chief items required for construction of the stand.

- (1) Several short lengths of board ($\frac{3}{4}$ inch thick)
- (2) Two strips of steel ($2\frac{1}{2}$ by $1\frac{1}{2}$ by $\frac{1}{8}$ inch)
- (3) Two cylindrical wire test tube baskets (6 inches in diameter and 6 inches high)

A wooden base is constructed by nailing the $\frac{3}{4}$ inch boards together to form a simple square platform measuring 20 by 20 inches. Each $2\frac{1}{2}$ inch metal strip is bent to a right angle, one arm measuring 24 inches in length and the other $11\frac{1}{2}$ inches. An opening ($\frac{3}{16}$ inch in diameter) is drilled in the 24 inch arm at a point 1 inch from the free end. A second drill hole is made 5 inches from the free end. A third opening is drilled 19 inches from the free end. Drill holes are made in the $1\frac{1}{2}$ inch arm at points $\frac{1}{2}$ and 1 inch from the free end respectively (Fig. 1).

The 24 inch metal arms are placed vertically parallel to one another and 5 inches apart over the central portion of the wooden base. These uprights are secured to the base by screws which pass through the two drill holes previously made in the $1\frac{1}{2}$ inch transverse arms. The upper wire basket is placed between the uprights and is bolted in position with its base lying 18 inches

above the wooden platform (The bolts fitted with large washers pass through the openings previously drilled 1 and 5 inches from the upper ends of the uprights) The lower basket is placed directly on the wooden platform between the uprights and is fixed in position by bolts which pass through the lowermost openings in the uprights. The stand now is complete and is ready to receive the bottles (Fig 1 B)

Discarded Vacoliter bottles (1000 cc) are used and will be found to fit into the baskets snugly. The bottles are connected as shown in Fig 2. The lower (water seal) bottle is securely wired or taped to its basket and remains in position permanently. The upper (catch) bottle is removable for purposes of emptying. Fig 3 shows the apparatus (old model) in use.

The setup described has the following advantages:

1. The base is sufficiently stable to prevent the apparatus from being accidentally overturned.

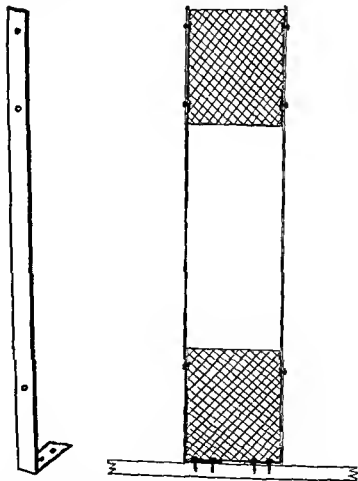


Fig 1.—A. Metal upright with drill holes in vertical and transverse arms. B. Diagrammatic side view of bottle stand. Metal uprights are fixed to wooden base by screws. Wire baskets are bolted to uprights through drill holes shown in A.

2 The fact that the catch bottle is supported only a short distance below the level of the patient makes it unnecessary to use a long connecting tube which is apt to become kinked and thus interfere with drainage.

3 The amount of drainage in the catch bottle can be read at a glance directly from the graduations on the Vacoliter flask.

4 The hydraulic resistance of the water seal remains constant for regardless of the amount of the run drainage into the catch bottle there is no entry of

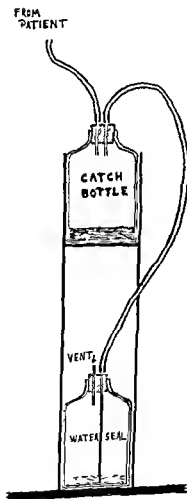


Fig 2

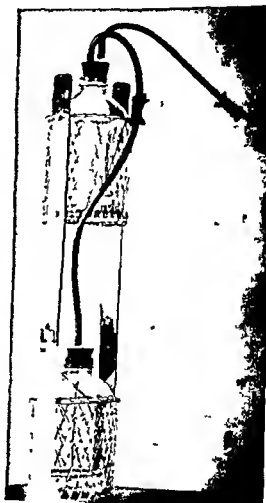


Fig 3

Fig 2.—Diagrammatic view of bottle showing connections. Stopper of catch bottle bears two short glass tubes. Long tube is immersed in water for a distance of only 4 to 5 inches. Water seal bottle is wired in place.

Fig 3.—Apparatus (old model) in use.

drainage fluid into the water seal bottle. (The lung tube of the seal bottle should be immersed in water for a distance of only $\frac{1}{4}$ to $\frac{1}{2}$ inch. Deeper immersion results in retardation of drainage from the chest.)

5 The bottles are maintained in a fixed position which prevents them from being inadvertently torn apart and the closed system thereby broken.

6 The height differential between the top of the catch bottle and the water seal is approximately 50 cm. which is sufficient to prevent aspiration of fluid from the seal bottle into the catch bottle and breaking of the seal on violent inspiration.

7 The lower (seal) bottle being wired in place cannot be elevated to a dangerous level by an uninitiated attendant thereby permitting its fluid to be aspirated into the catch bottle and the seal thus broken.

8 If desired the entire stand can be elevated for inspection of both bottles without influencing the height differential between them and running the risk of breaking the seal. Furthermore if the stand is elevated there is no danger of fluid in the catch bottle being aspirated into the pleural cavity.

9 Negative pressure can be readily applied to the system if desired merely by connecting a suction apparatus to the vent in the water seal bottle.

Personal experience over a period of two years demonstrated the apparatus to be eminently satisfactory in maintaining an effective water seal under circumstances which at times permitted only minimal supervision.

Case Reports

BENIGN FIBROMUCOUS POLYP OF THE URETER

REPORT OF A CASE

JAMES K. PALMER, M.D.,* AND LAURENCE F. GREENE, M.D.† ROCHESTER, MINN.

VEST,[‡] in 1945 reported that he was able to find only seventy odd cases of ureteral tumor which were considered to be benign. Of these tumors, he estimated that 60 per cent occurred in the lower part of the ureter and that 30 to 35 per cent protruded from the ureteral orifice. The diagnosis of these tumors as described in the literature, is based on the clinical symptoms of renal or ureteral pain, with or without extension and, in some instances, gross hematuria. The hematuria may be microscopic, and in some cases a hydronephrotic kidney secondary to the ureteral tumor may be palpable. Roentgenographic studies may disclose a filling defect in the excretory or retrograde urogram, an minimal or marked hydronephrosis. In some cases a mass protruding from one of the ureteral orifices may be seen by cystoscopic examination. Unilateral hematuria and obstruction or bleeding at a localized point on attempted passage of a ureteral catheter may also be noted. Careful microscopic examination of the excised lesion is necessary to establish the benign nature of the tumor. Because of the relatively infrequent occurrence of such benign lesions of the ureters we report the following case.

REPORT OF A CASE

The patient, a woman 34 years old, complained of intermittent episodes of gross hematuria of nine years' duration. During this period she had had fifteen episodes of gross hematuria, each of which had lasted four or five days, the last episode occurring three months before admission to the Mayo Clinic. She described one attack of excruciating pain in the right lumbar region which extended to the groin and required narcotics for relief. She had had episodes of urinary urgency and frequency for as long as she could remember. The remainder of her history and the results of physical examination were noncontributory, neither kidney was palpable.

Results of routine laboratory studies were normal or negative. Urinalysis was reported to disclose pyuria of grade 1 (on the basis of 1 to 4). An excretory urogram was made and interpreted as revealing nothing abnormal. At first glance the bladder and both ureteral orifices seemed normal in cystoscopic examination. However study of the right ureteral orifice disclosed a narrow polypoid lesion, 0.75 cm. in diameter, which with each ejaculation of urine, protruded 15 cm. into the bladder from the right ureteral orifice. The gross appearance of the polyp suggested a benign lesion. The right ureter was easily catheterized. A right pyelo ureterogram was made (Fig. 1). This was interpreted as indicating that the right kidney and ureter were normal except that poor visualization of the lowermost portion of the ureter suggested that it was dilated.

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†Vest, J. A. Conservative Surgery in Certain Benign Tumors of the Ureter. *J. Urol.* 53

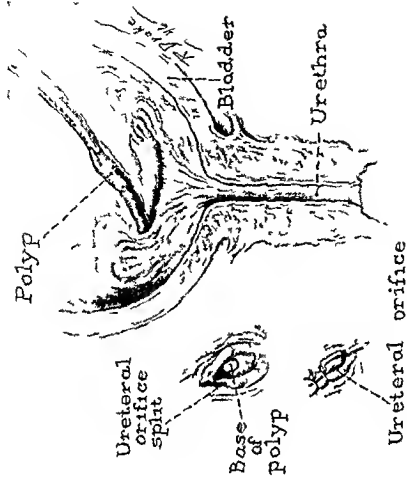


Fig. 1

Fig. 1—The dilatation of the lower part of the ureter



Fig. 1

Fig. 1—The resected specimen

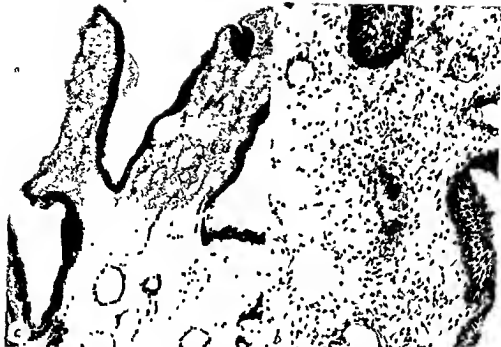


Fig. 3—Low (a X40) and high (b X160) magnification of tissue from the ureteral polyp. The polyp was lined by squamous and transitional epithelium thrown into papillary folds and was comprised of very vascular myxomatous connective tissue (hematoxylin and eosin stain).



Fig. 4—a Postoperative excretory urogram showing normal urinary tract. b postoperative right retrograde pyelogram.

Transvesical excision of the polyp was advised and carried out. The bladder was opened in the midline. The polyp could be seen periodically projecting from the right ureteral meatus. At times, this polyp was completely retracted up the ureter. A small curved hemostat was passed up the right ureter, and the polyp was grasped and pulled down until its base appeared near the ureteral meatus (Fig 2). The meatus was then incised upward for 1 cm to expose the base of the polyp (Fig 2). The polyp was then completely excised and the ureteral meatus was reconstructed with two catgut sutures (Fig 2). The bladder was closed about a No. 26 French cystostomy tube.

The specimen consisted of a polypoid lesion 4 by 0.7 cm. Multiple sections were made and examined microscopically. These showed benign fibromuscular tissue covered with normal squamous epithelium (Fig 3, *a* and *b*).

The patient withstood the surgical procedure well. Convalescence was uneventful.

At our request the patient returned nine months later for re-examination. Her health had been perfect and she had no urinary symptoms. The urinary tract was studied by means of excretory urography, cystoscopy, and retrograde pyelography, and was considered to be normal (Fig 4, *a* and *b*).

UNILATERAL, CONGENITAL SYNOSTOSIS OF LUNATE AND TRIANGULAR BOYES

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CONGENITAL fusion of carpal bones is not common and the infrequency of synostosis of the lunate and triangular bones warrants the following case report

CASE REPORT

A white, American soldier, aged 20 years, was admitted to the 24th General Hospital, U S Army, on June 19, 1945, complaining of a fracture of the fifth metacarpal of the left hand. On June 5, 1945, a rifle which he was cleaning accidentally discharged and caused a perforating wound of the left hand. A ray examination revealed a comminuted fracture of the proximal shaft and base of the fifth metacarpal. On June 6, 1945, debridement was done and a short arm cast was applied.

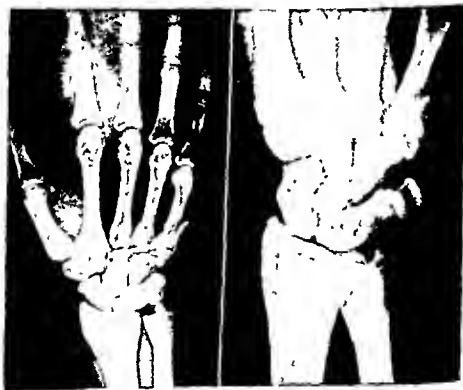


Fig 1—Anteroposterior and oblique roentgenograms of the left wrist showing the carpal anomaly

A review of the x ray films revealed that in addition to the fracture described there was an interesting anomaly of the carpus consisting of fusion of the lunate and triangular bones (Fig 1). Roentgenogram of the right wrist did not reveal a similar synostosis.

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Detailed questioning of the patient failed to disclose any symptoms referable to the left wrist prior to wounding.

A review of the literature reveals the following points of interest concerning this carpal anomaly. Congenital synostosis of the triangular and lunate bones causes no symptoms and cannot be recognized by clinical examination. Most cases are discovered accidentally in roentgenograms taken for other conditions. It most commonly occurs bilaterally. The fusion is generally complete rather than partial. Synostosis of tarsal bones may accompany. The frequent symmetrical distribution of synostoses of the carpus and tarsus, their association with synostoses or aplasia of the interphalangeal joints, and the familial occurrence of these anomalies tend to indicate a congenital and hereditary character of the lesions.

Most authors agree that the underlying cause is an absence or imperfect differentiation of the intermediary zone in the development of the ossification centers for the carpus. Fusion of such bones is a result of hypoplasia or aplasia of the individual articulations.

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Book Reviews

Cancer—Diagnosis Treatment and Prognosis By Lauren V. Ackerman and Juan A. del Regato. Pp 1115 with 745 illustrations and 42 color reproductions. St. Louis 1941. The C. V. Mosby Company.

The work by Ackerman and Regato is excellently done. It is rather difficult for the reviewer to see how a consideration of so broad a subject as cancer could be so well handled. Malignant diseases involving the various regions of the body are very carefully considered from the standpoint of etiology, symptomatology, treatment, and prognosis. It is remarkable also, how judicious the authors have been in evaluating the various forms of therapy particularly surgery and irradiation. The volume is profusely illustrated not only with photographs of lesions and tissues which are well reproduced but also colored photographs of lesions. An important part of the book is the diagrammatic demonstration of the lymph drainage of each malignant lesion discussed. The work is particularly valuable from the standpoint of teaching and of value to the clinician in handling the patient with malignant disease. In addition to the specific consideration of treatment in each type of malignancy, a chapter is devoted to the general consideration of surgery of cancer and another one to radiotherapy of cancer. These are concerned primarily with the broad application of these two therapeutic agents. Appended to each chapter is an excellent bibliography which is quite complete.

After a careful review of this volume it is difficult to say if there is any one part that is better than the others. Every subject seems to be well handled and thoroughly covered. This is a book which should be in the hand of every practitioner who is concerned with the diagnosis and treatment of malignancies. In fact every doctor could well afford to have this in his library because of its value as a reference book.

BOOKS RECEIVED

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

HARVY CUSHING A BIOGRAPHY By John F. Fulton M.D. Sterling Professor of Physiology, Yale University. Cloth. Pp. 18 with 150 illustrations. Springfield Ill 1940, Charles C Thomas Publisher.

DIAGNOSIS AND TREATMENT OF MENSTRUAL DISORDERS AND STERILITY By Charles Mazet M.D., Assistant Professor of Gynecology and Obstetrics University of Pennsylvania and S. Leon Israel M.D. Instructor University of Pennsylvania. Cloth. Price \$7.50. Pp. 213 with 133 illustrations. New York 1940 Paul B. Hoeber Inc.

SURGICAL TREATMENT OF SOFT TISSUES By Frederic W. Barcroft M.D. F.A.C.S., Associate Clinical Professor of Surgery Columbia University and George H. Humphreys, M.D., F.A.C.S., Valentine Mott Professor of Surgery Columbia University. Cloth. Price \$10. Pp. 261 with 234 illustrations. Philadelphia 1941 J. P. Lippincott Company.

URGENT SURGERY, Volume I By John I. Sprueck M.D. LL.D. Associate Professor of Surgery, University of Illinois. Cloth. Price \$10. Pp. 171 with 71 illustrations. Springfield Ill, 1940 Charles C. Thomas Publisher.

NEUROANATOMY By Fred A. Mettler, Ph.D. Professor of Anatomy, University of Georgia School of Medicine. Cloth. Pp. 384 with 137 illustrations. St. Louis 1946, The C. V. Mosby Company.

CURRENTS IN BIOCHEMICAL RESEARCH By David E. Green. Chief of the Enzyme Laboratory, Columbia University, Editor. Cloth. Price \$6. Pp. 486 with no illustrations. New York 1947. Interscience Publishers, Inc.

INTRODUCTION TO SURGERY By Virginia Kneeland Frazier, M.D., Associate Professor of Surgery, Columbia University and Harold Dorte Harvey, M.D., Assistant Professor of Clinical Surgery, Columbia University. Cloth. Pp. 208 with 11 illustrations. New York 1946. Oxford University Press.

PENICILLIN IN NEUROLOGY By A. Earl Walker, M.D., Associate Professor and Herbert C. Johnson, M.D., Resident Neurological Surgeon, University of Chicago. Cloth. Price \$3. Pp. 177 with 72 illustrations. Springfield, Ill. 1946. Charles C. Thomas Publisher.

OUTLINE OF THE SPINAL NERVES By John Favill, A.B., M.D., F.A.C.S., Clinical Professor of Neurology (Rush) University of Illinois. Cloth. Price \$3.75. Pp. 191 with 12 illustrations. Springfield, Ill. 1946. Charles C. Thomas Publisher.

THE COMING OF THE PEDIATRICIAN Dr. W. C. David, M.D., Professor of Pediatrics, Duke University School of Medicine. Cloth. Price \$3.75. Pp. 100 with no illustrations. Durham, N. C. 1946. Duke University Press.

POSTGRADUATE OBSTETRICS By William F. Mengert, M.D., Professor of Obstetrics and Gynecology, Southwestern Medical College. Price \$5. Pp. 363 with 12 illustrations. New York 1947. Paul B. Hoeber Inc.

AN INTEGRATED PRACTICE OF MEDICINE. FOUR VOLUMES AND INDEX By Harold Thomas Hyman, M.D. Cloth. Pp. 4131 with 1184 illustrations. Philadelphia 1947. W. B. Saunders Company.

INTESTINAL ALIMENTATION IN SURGERY By Robert Elman, M.D., Associate Professor of Clinical Surgery, Washington University School of Medicine. Cloth. Price \$4.50. Pp. 96 with 32 illustrations. New York 1947, Paul B. Hoeber Inc.

GYNECOLOGICAL AND OBSTETRICAL PATHOLOGY By Emil Novak, A.B., M.D., D.Sc., F.A.C.S., Associate in Gynecology, Johns Hopkins Medical School. Cloth. Pp. 425 with 24 illustrations. Philadelphia 1947. W. B. Saunders Company.

HEPARIN IN THE TREATMENT OF THROMBOSIS By J. Erik Jorpes, M.D., Reader in Biochemistry, Carolinska Institute, Stockholm, Sweden. Cloth. Price \$6.50. Pp. 9 with 21 illustrations. New York 1947. Oxford University Press.

PHYSICAL MEDICINE IN GENERAL PRACTICE By Arthur I. Watkins, M.D. Cloth. Price \$6. Pp. 130 with 8 illustrations. Philadelphia 1947. J. B. Lippincott Co.

RADICAL SURGERY IN ADVANCED ABDOMINAL CANCER By Alexander Braun, M.D., Professor of Surgery, University of Chicago. Cloth. Price \$7.50. Pp. 18 with 11 illustrations. Chicago, 1947. University of Chicago Press.

FUNDAMENTALS OF CLINICAL NEUROLOGY By H. Houston Merritt, M.D., Professor of Clinical Neurology, University of Illinois, Chicago, Illinois, and Fred A. Mettler, M.D., Associate Professor of Clinical Neurology, University of Tennessee, Knoxville, Tennessee. Cloth. Pp. 311 with 92 illustrations. New York 1947. The McGraw-Hill Company.

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CLFFT PALATE AND SPEECH By Muriel E. Morley, B.Sc., F.C.S.T., Speech Therapist to Royal Victoria Infirmary Cloth Price \$3 Pp 154 with 52 illustrations Edinburgh, 1945, E & S Livingstone

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SURGERY OF THE HAND By B. M. Handfield Jones, M.C., M.S., F.R.C.S., Examiner in Surgery, Universities of Cambridge Cloth Price \$5.50 Pp 156, with 104 illustrations Baltimore, 1946, Williams & Wilkins Company

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SURGICAL PATHOLOGY By William Boyd, M.D., Professor of Pathology, University of Toronto Cloth Pp 820 with 520 illustrations Philadelphia 1947, W. B. Saunders Company

GYNECOLOGY WITH A SECTION ON FEMALE UROLOGY By Lawrence B. Wharton, Ph.D., M.D., Assistant Professor of Gynecology, Johns Hopkins Medical School Cloth Pp 1,000, with 479 illustrations Philadelphia 1947, W. B. Saunders Company

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SURGERY

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Original Communications

SYMPATHECTOMY AS AN ADJUVANT IN THE OPERATIVE TREATMENT OF ANEURYSMS AND ARTERIOVENOUS FISTULAS

I SYMPATHECTOMY PERFORMED BEFORE OR AT TIME OF OPERATION

HARRIS B. SHUMACKER JR. MD, NEW HAVEN, CONN.

(From the Vascular Center, Mayo General Hospital, Galesburg, Ill. and the Department of Surgery, the Yale University School of Medicine, New Haven)

GAGE¹ and BIRD² in 1934 independently utilized sympathetic interruption as a preliminary procedure before surgical extirpation of an aneurysm, the former by alcohol injection, the latter by ganglionectomy. Although impressed with the apparent benefit of sympathectomy in rendering the collateral circulation more efficient, Bird presented this contribution with definite reservations, being hopeful at that time that the recently introduced paxton might make unnecessary other efforts to foster development of collateral circulation. Gage on the other hand felt convinced that sympathetic interruption would maintain a prominent place in the surgical management of aneurysms. He and Ochsner subsequently reported additional successful experiences with this procedure.^{3,4} From time to time a number of other papers have appeared describing the use of sympathectomy before or at the time of operation for the cure of aneurysm.⁵⁻¹²

All of the relatively few cases thus far reported in the literature have been successful, what was considered adequate circulation following in each case an operation which had necessitated ligation of the affected artery. Because of this fact I believe that one derives from these papers perhaps contrary to the intent of their authors, the impression that sympathectomy is an almost impregnable defense against ischemic disaster in the treatment of vascular lesions requiring ligation of main arteries. My own experience certainly confirms the general usefulness of this procedure and yet makes evident certain limitations. It is the purpose of this communication to record a rather large experience with sympathectomy in cases of aneurysm and arteriovenous fistula to point out its merits and its limitations and to attempt to formulate a proper plan for its intelligent use as an adjuvant in the operative treatment of such

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cases. For the sake of simplicity, the problem will be divided into two parts. The use of sympathectomy before or at the time of operation for these lesions will be presented in this paper; the use of this procedure in an effort to correct certain circulatory difficulties following the operative cure of aneurysms and fistulas will be presented in another paper.¹¹

There is ample experimental and clinical evidence to support the view that sympathectomy may be of definite help in maintaining the best possible circulation in various conditions in which the continuity of blood flow through important arterial trunks has been interrupted. Sympathectomy could conceivably be helpful in such cases by two mechanisms: the first of which is well established, whereas the second is hypothetical and requires considerable investigative support before it can be considered factual. In the first place, by eliminating vasoconstrictor impulses and contributing to the maintenance of near maximal circulation, sympathectomy should ensure the fullest use of the existing collateral circulation. In the second place, as has been suggested, it might possibly aid in bringing about more rapid growth of new collateral channels through reduction in peripheral resistance to blood flow, or through some other means.

Indeed, one might readily defend the point of view that sympathectomy should be performed in every case in which there is an aneurysm or a fistula, the cure of which might entail ligation of an important arterial stem. On the other hand, clinical experience has demonstrated that large numbers of aneurysms and fistulas can be extirpated without serious resultant ischemic difficulties, provided careful testing of the collateral circulation is used as a guide in the selection of the proper time for operation and provided the operation is carried out with extreme care so that no collateral vessels are needlessly sacrificed. Thus, some investigators have held that sympathectomy should be used almost uniformly in such cases; others have believed that one need rarely, if ever, resort to this procedure. In the cases on which the present study is based it has been my practice to follow a course somewhat between these two views. Sympathectomy has been utilized whenever it might reasonably be expected to result in definite benefit to the patient. Undoubtedly, the procedure has been used more often than was necessary to prevent gangrene, for example. I have kept in mind, however, the fact that study of an extensive series of sympathectomies might permit a more rational evaluation of the procedure in the future, and I was convinced that if clear-cut benefit did not follow in every instance at least no harm would result.

INDICATIONS FOR SYMPATHECTOMY AND CLINICAL MATERIAL

The chief indications which have been followed in selecting cases for sympathectomy were: (1) Evidence of poor collateral circulation in patients with lesions sufficiently old to have produced, under ordinary circumstances, a fairly efficient collateral circulation. (2) The coexistence of inadequate collateral circulation and of peripheral nerve injuries requiring surgical exploration. Since early surgical treatment of peripheral nerve injuries results in better return of function than late treatment of such lesions, it is my conviction

that every effort should be made to increase the efficiency of the collateral circulation to permit as early operation as possible. In such cases it is hazardous to explore a nerve before treatment of the aneurysm or fistula, and it is ordinarily feasible to carry out both procedures concomitantly. (3) The impossibility of testing the collateral circulation in certain cases in which an important arterial trunk appears to be involved. In occasional cases the affected artery cannot be compressed at the site of the fistula or aneurysm, hence, no accurate testing of the collateral circulation is possible. (4) The presence of ischemic lesions associated with aneurysm or fistula. (5) Intense vasospasm in the affected limb, or a rather severe generalized vasospastic disorder. (6) The loss of one or more major arteries by previous injury or operation in a limb in which the cure of an aneurysm or fistula will likely necessitate ligation of other important arterial channels. (7) Causalgia in the affected limb relieved temporarily but not cured by sympathetic blocks.

In the present series of cases * 290 aneurysms and arteriovenous fistulas were operated upon. An additional 13 cases required no operative treatment because of spontaneous cure of the lesion by thrombosis. In this group of 303 cases 78 sympathectomies were carried out before or at the time of operation. One additional sympathectomy should properly be included since it was performed in a patient thought to have an aneurysm the signs of which were found subsequently to be due to costoelavicular compression of the subclavian vessels.¹² Of these 79 sympathectomies 24 were dorsal and 55 lumbar sympathectomies. Lumbar sympathetic ganglionectomies were performed under spinal anesthesia through an anterior extraperitoneal muscle splitting incision. The upper extremities were denervated by the preganglionic operation of Smithwick performed under intratracheal gas oxygen ether anesthesia. No deaths and no serious complications occurred.

In Table I are summarized data concerning the distribution of cases according to the affected artery. Not included are two cases in which satisfactory 'cure' of the lesion by thrombosis followed sympathectomy and the case mentioned previously in which the patient was found to have no aneurysm. It is

TABLE I SYMPATHECTOMY PERFORMED BEFORE OR AT TIME OF OPERATION FOR ANEURYSM OR ARTERIOVENOUS FISTULA

SITE OF LESION	ARTERIAL ANEURYSM					
	NO OF PATIENTS OPERATED UPON					
Innominate	1					
Subclavian	5	1	20	6	2	33.3
Axillary	13	7	53.8	12	4	33.3
Brachial	22	3	13.6	11	2	18.2
Common femoral				3	2	66.7
Femoral	6	3	50	47	14	29.8
Iliac	16	12	75	41	13	31.7
Other	21	2	9.5	80	10	11.6
Total	84	29	34.5	106	44	22.6

* All but two were treated at the Mayo General Hospital; the others were treated subsequently at the Johns Hopkins Hospital.

apparent from the data recorded that the majority of sympathectomies were carried out in patients with lesions of the larger peripheral arterial stems. Sympathectomy was performed in 23 of 57 cases of popliteal involvement (40 per cent), in 11 of 25 cases of axillary lesions (44 per cent) in 17 of 53 cases of femoral aneurysm or fistula (32.1 per cent) in 3 of 11 cases of subclavian (27.3 per cent), and in 5 of 33 cases of brachial lesions (15.1 per cent). A few sympathectomies were done in instances of involvement of the innominate or common femoral artery. In 12 of the 107 cases with involvement of vessels other than those just mentioned sympathectomy was performed (11.2 per cent).

As will be developed subsequently a number of these latter cases were instances in which preoperative studies erroneously suggested involvement of an important artery near the affected vessel. Altogether 76 sympathectomies were performed in the 290 cases in which operative treatment of the aneurysm or fistula was necessary (26.2 per cent).

Sympathectomy was performed in a larger percentage of arterial aneurysms (34.5 per cent) than in cases of arteriovenous fistula (22.6 per cent). This difference is more apparent upon consideration of the axillary, femoral and popliteal lesions those for which sympathectomy was most frequently done. The percentage of arterial aneurysms in which sympathectomy was performed for these lesions was 53.8, 50 and 75, whereas the percentage of arteriovenous fistulas in which sympathectomy was carried out for these lesions was 33.3, 29.8 and 31.7. Although this difference is primarily a reflection of the tendency to poorer collateral circulation in instances of arterial aneurysm it is partly dependent upon the fact that associated nerve injuries requiring operative treatment were twice as common in cases of arterial aneurysms as in those of arteriovenous fistula. It is not due to a higher incidence of lesions of these major arterial stems in cases of arterial aneurysm. Forty-eight per cent of the arterial aneurysms operated upon involved the subclavian, axillary, femoral and popliteal arteries. In 53 per cent of the arteriovenous fistulas there was involvement of these vessels.

RESULTS OF THE PROCEDURE

In Tables II to VIII are recorded data upon the patients who have had sympathectomy before or at the time of operation for aneurysm or fistula. An effort has been made to segregate them into groups according to the chief indication for the procedure. It should be pointed out that in certain instances sympathectomy was decided upon not because of a single reason but because of a combination of reasons. Such relevant data as are consistent with brevity are included in the tables.

SYMPATHECTOMY PERFORMED BECAUSE OF POOR COLLATERAL CIRCULATION

In Tables II and III are summarized data regarding 31 patients upon whom sympathectomy was performed because of poor collateral circulation. In these cases and in all others included in this study the state of the collateral circulation was investigated by repeated use of a number of tests and observations but chief reliance was placed upon the reactive hyperemia test of Matas. My

experience with these tests has been reported elsewhere¹⁸ To simplify interpretation of the results of sympathectomy those cases in which the tests showed that the collateral circulation was satisfactory after sympathectomy are grouped in Table II those in which the tests did not reveal adequate collateral circulation are placed in Table III

In a number of these patients it will be seen that in addition to evidence of poor collateral circulation there were other reasons why it was deemed advisable to make every effort to render the collateral circulation adequate as rapidly as possible For example in 16 or 41 per cent there were present associated peripheral nerve lesions requiring operative treatment In others there was severe pain or pronounced vasospasm and in one case there was superficial gangrene In 34 or 87 per cent the aneurysm or fistula was of three months duration or longer before sympathectomy was performed and in 18 of them (46 per cent) the lesion was of five months duration or longer In the five cases in which sympathectomy was performed earlier specific indications were present which made it advisable I felt to proceed with sympathectomy without further delay Two patients (Cases 6 and 18 Table II) had severe pain In one of them a popliteal aneurysm had ruptured subcutaneously and it was obvious that further increase in the size of the aneurysm might necessitate operation at any moment In the other patient in addition to severe causalgia which was associated with a femoral arteriovenous fistula with sacular aneurysm and peroneal paralysis and which had necessitated the use of narcotics to the point of real danger of addiction there was a compound comminuted fracture of the femur intense vasospasm of the foot an ulcer of the heel and superficial gangrene of the toes In both patients the pain was diminished or relieved and the tests for collateral circulation became adequate shortly after sympathectomy A third patient (Case 20 Table II) with a popliteal fistula of two and one half months duration had extremely poor collateral circulation and complete peroneal paralysis The collateral circulation became adequate after sympathectomy permitting early treatment of the aneurysm and the nerve lesion The two other cases (Cases 3 and 4 Table III) were instances of a femoral and a popliteal aneurysm of two months duration in which the tests for collateral circulation were extremely poor In neither case did these tests become satisfactory after operation although they showed some improvement In one patient spontaneous cure took place and in the other operative treatment two months after sympathectomy was followed by an excellent result In all of the patients some intermittent proximal occlusion of the involved artery had been practiced without apparent improvement in collateral circulation In only a few however had this method been given a prolonged trial

In Table II are grouped twenty five patients in whom the previously poor results of testing the collateral circulation became satisfactory after sympathectomy The interval between sympathectomy and operation upon the aneurysm or fistula did not necessarily correspond to the interval between sympathectomy and the time when these tests became adequate Some of the patients were allowed to return home on sick leave between operations In some the second operation was deferred because of an unrelated illness such as malaria

TABLE II SYMPATHECTOMY PERFORMED BEFORE OPERATION FOR ANEURYSM OR FISTULA, INDICATION—POOR COLLATERAL CIRCULATION, CASES IN WHICH TESTS FOR COLLATERAL CIRCULATION BECAME SATISFACTORY AFTER SYMPATHECTOMY

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPATHECTOMY (IN MO)	INTERVAL BETWEEN SYMPATHECTOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Arterial Aneurysm</i>						
1	Axillary	3	2	E	Also had brachial plexus injury requiring neurolysis	Good, has some cold sensitivity
2	Brachial	5.5	5	E	Also plexus injury requiring lysis	Excellent
3	Brachial	5	2	E	Also median and ulnar palsy, median lysis, ulnar neurotomy	Excellent
4	Brachial	3	10	A E	Also plexus injury requiring lysis tests for collateral circulation did not become satisfactory for 2 mo	Excellent
5	Femoral	5.5	1	L		Excellent
6	Popliteal	2	3	A	Very large, subcutaneous rupture severe pain, pain less after sympathectomy	Excellent
7	Popliteal	5	3	A		Excellent
8	Popliteal	5.5	5	A		Excellent
9	Popliteal	--	1.5	A	Arteriosclerotic aneurysm	Excellent
<i>Cases of Arteriovenous Fistula</i>						
10	Subclavian	5	3	E	Also ulnar palsy, requiring lysis	Excellent
11	Axillary	3	2.5	E	Also plexus injury, lysis radial neurotomy, hand cold, blue before sympathectomy, circulation strikingly improved	Excellent
12	Axillary	5	3.5	F	Also plexus injury requiring lysis	Excellent
13	Axillary	6.5	2	E		Excellent

or gastroenteritis. It is seen however that in most instances the operation upon the vascular lesion followed closely the sympathectomy. In 10, or 40 per cent, it was done within two weeks; in 17 or 68 per cent, in three weeks or less, and in 20, or 80 per cent in four weeks or less. In only five instances was it delayed five weeks or more. In one of these (Case 18) the tests for collateral circulation became adequate shortly after sympathectomy but operation was deferred because of a compound fracture of the femur and infected ulcers of the foot. In the other four cases the tests for collateral circulation showed steady improvement after sympathectomy.

It will be noted that 25 of the 39 patients (64 per cent) upon whom sympathectomy was performed because of inadequate circulation showed evidence of satisfactory collateral circulation after this procedure and that in the majority of them these tests were adequate very shortly after operation. It will also be noted that there was no great difference in this respect between the group of arterial aneurysms and that of arteriovenous fistulas. Nine of 15 patients with arterial aneurysm (60 per cent) and 16 of 24 with fistulas (66.7

TABLE II (CONT'D)

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPA THEC TOMY (IN MO)	INTERVAL BETWEEN SYMPA THEC TOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
14	Axillary	6.5	3	E	Also plexus injury, ulnar and radial neurotomy necessary	Excellent
15	Brachial	3	7.5	E	Also ulnar and median palsy requiring lysis, collateral circulation tests very poor before good after sympathectomy	Excellent
16	Common femoral	5.5	1	E		Excellent
17	Femoral	3	2	E		Excellent
18	Femoral	2.5	21	E	Also peroneal palsy, FOC femur and pain, tests for collateral circulation adequate shortly after sympathectomy, burning pain disappeared	Excellent
19	Femoral	3	4	E R	Tests for collateral circulation improved progressively over period of several weeks after sympathectomy	Excellent, successful vein graft to arterial defect
20	Popliteal	2.5	2	E	Also peroneal palsy	Excellent
21	Popliteal	2.5	1.5	E	Also pronounced vasospasm	Excellent
22	Popliteal	3.5	2	E	Also peroneal palsy requiring suture	Excellent
23	Popliteal	4	3	E	Collateral circulation thought adequate after sympathectomy	Poor, gangrene of the distal third of the foot
24	Popliteal	10	3	E	Also peroneal palsy	Excellent
25	Popliteal	9	4	E R		Excellent, continuity of artery maintained, ligation of fistula

Abbreviations used in this and the following tables

E Ligation

E R Excision with restoration or maintenance of continuity of affected artery

A Aneurysmorrhaphy or aneurysmotomy with intrasacral ligation of transfixing arteries

A E Aneurysmorrhaphy or similar procedure followed by excision of the sac

A E R Aneurysmorrhaphy or similar procedure followed by excision of the sac and by restoration of continuity of the artery

per cent) showed evidence of good collateral circulation after sympathectomy, according to the reactive hyperemia test and other tests

In all save two of the cases listed in Table II, cure of the aneurysm or fistula entailed ligation of the affected artery. In the exceptions (Cases 19 and 25) continuity of the artery was preserved or re-established by ligation of the fistula or by vein graft to bridge the arterial defect. In these and in the other tables where the result is said to be excellent, the limb maintained normal warmth and color under ordinary environmental conditions, no significant or

TABLE III SYMPATHECTOMY PERFORMED BEFORE OPERATION FOR ANEURYSM OR FISTULA,
INDICATION—POOR COLLATERAL CIRCULATION, CASES IN WHICH TEST FOR COLLATERAL
CIRCULATION DID NOT BECOME SATISFACTORY AFTER SYMPATHECTOMY

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPATHECTOMY (IN MO)	INTERVAL BETWEEN SYMPATHECTOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Arterial Aneurysm</i>						
1	Axillary	3.5	9	A E R	Also plexus injury requiring lysis	Excellent successful end-to-end suture
2	Brachial	4	6.5	A E	Also plexus injury requiring lysis and radial neurotomy	Excellent
3	Femoral	2		None	Thrombosis occurred after sympathectomy with gradual obliteration of sac	Excellent
4	Popliteal	2	8.5	A		Excellent
5	Popliteal	4	15	A		Excellent
6	Popliteal	--	17	E R	Aneurysm due to median artery circulation in foot poor before good after sympathectomy	Excellent successful vein graft
<i>Cases of Arteriovenous Fistula</i>						
7	Femoral	3.5	30	E R	Collateral circulation improved after sympathectomy but never satisfactory	Excellent continuity artery maintained, fistula ligated
8	Femoral	7	5	E R	Collateral circulation tests improved markedly after sympathectomy became questionable adequate	Excellent continuity artery maintained, fistula ligated
9	Femoral	5	9	E R C		Excellent continuity artery maintained, fistula ligated
10	Popliteal	3.5	10	E R	Tests for collateral circulation improved markedly after sympathectomy never entirely satisfactory	Excellent continuity artery maintained, fistula ligated
11	Popliteal	6.5	10	E R	Also peroneal palsy requiring suture tests for collateral circulation improved but never became satisfactory	Excellent continuity artery maintained, fistula ligated
12	Popliteal	5	5	E R	Tests for collateral circulation improved but never became completely satisfactory	Excellent continuity artery maintained, fistula ligated
13	Popliteal	11	3.5	E	Tests for collateral circulation improved but never became satisfactory	Excellent
14	Popliteal	5	13	E R	Tests for collateral circulation improved slightly but never became satisfactory	Excellent continuity artery maintained, fistula ligated

disturbing sensitivity to cold existed, and there was satisfactory evidence of return of nerve function. If follow-up of the patient was not continued long enough to permit restoration of sensation and motor power, at least evidence, such as progression distally of the point at which Tinel's sign might be elicited, showed satisfactory improvement comparable to cases in which no vascular disorder existed. Naturally there was no regeneration of those nerves in which apparently irreparable damage had occurred and in which no reparative procedure could be carried out. Where speaking of an excellent result, I do not mean to imply that no fatigue on exercise was present, for this finding was invariably noted in cases in which such arteries as the femoral or popliteal had been ligated. One patient (Case 1) had some cold sensitivity following operation, in which it was necessary to ligate the axillary artery. In one instance gangrene occurred.

CASE REPORT

CASE 23 (Table II).—The patient was a 35-year-old soldier who had signs of popliteal arteriovenous fistula. There was no flush during the reactive hyperemia test. Four months after injury sympathectomy was performed. Immediately after this procedure the tests for collateral circulation showed definite improvement. The flush appeared promptly after deflation of the constricting cuff and steadily improved so that it was full and complete in two minutes, showing no further improvement upon release of pressure from the popliteal artery. Similar results were obtained on several occasions. The fistula was explored three weeks after sympathectomy. In addition to a large communication between the popliteal artery and vein there was also a small sacular aneurysm of the popliteal artery from which emerged a large geniculate branch. This branch had to be ligated in the excision of the lesion, and it appeared likely that the fistula had been occluded during the preoperative tests without interrupting blood flow through this branch, thus giving misleading information concerning the state of the collateral circulation.¹⁴ The drapes were not applied in such a way as to keep the foot in view during the operative procedure, a precaution which is essential in every instance in which doubt exists of the adequacy of the collateral circulation. This precaution was unfortunately omitted as the result of a false sense of security which prevailed because up to this point no ischemic difficulty had occurred in a sympathectomized limb and there had been no experience to suggest that the reactive hyperemia test might give misleading information. At the completion of operation the foot had poor color and warmth and within a few days gangrene was apparent, necessitating amputation of the distal third of the foot.

This case is cited in some detail because it illustrates the fact that sympathectomy offers no guarantee against ischemic disaster because it shows the occasional fallibility of tests for collateral circulation, and because it makes obvious the necessity for every care and precaution. It is of interest that with the exception of one case in which gangrene followed thrombosis which occurred on the sixth postoperative day in a limb which had previously shown excellent circulation this is the only case in my experience of gangrene following surgical treatment of an aneurysm or fistula. This experience includes fifty-seven cases of femoral and fifty-seven cases of popliteal lesions cured by surgical means.

In Table III are summarized the fourteen cases in which sympathectomy failed to render the tests for collateral circulation satisfactory. In every instance there was some improvement in these tests after sympathetic interrup-

tion. In some the tests became definitely better but in none did they become adequate according to the standards which I feel should be followed as indicating reliably efficient collateral circulation.¹⁴ It will be noted that in these cases a longer interval elapsed between sympathectomy and operation upon the aneurysm or fistula than in those cases listed in Table II. In only a single instance was this interval less than five weeks and in nine or 64.3 per cent it was two months or longer. It will also be seen that in one patient a satisfactory cure by thrombosis occurred making operation unnecessary and that in nine patients the continuity of the affected artery was maintained or restored by ligation of the fistula by end-to-end suture or by vein transplant. In only four or 28.6 per cent was it necessary to ligate the involved artery. In all cases an excellent result was obtained. The limbs maintained good color and warmth and there was no sensitivity to cold. Nerve return progressed satisfactorily when a peripheral nerve paralysis had been present. In those cases in which the continuity of blood flow through the affected artery was successfully maintained there was in addition no fatigue on exercise unless such fatigue had been present before operation.

In all cases the color and warmth of the affected hand or foot was observed during a prolonged period of precise occlusion of the artery with a rubber shod clamp at the time of operation. In all instances save one this period of observation showed that the collateral circulation was actually adequate al

that

explained adequately the reason for the false results of the tests carried on before operation for example the presence of some large collateral vessels which would necessarily have been occluded during digital compression but which could be preserved at operation.¹⁵ That the collateral circulation was apparently actually satisfactory in all save the one case referred to and probably the one case in which operation was unnecessary does not necessarily signify that it had been rendered so by sympathectomy. All that can be said is that the same tests for collateral circulation before and after sympathectomy showed some improvement in all instances after this procedure and great improvement in some but that they did not become completely satisfactory in any.

In Tables II and III four types of response to sympathectomy occurred. In some cases the tests for collateral circulation became adequate immediately or shortly after sympathectomy. In some the tests showed significant improvement soon after sympathectomy with slow steady improvement until they became satisfactory some weeks later. In others the tests improved somewhat but never became adequate. In most of these more precise tests performed with the lesion exposed at operation demonstrated that the collateral circulation actually was satisfactory although in one instance such tests confirmed the inadequacy of the collateral circulation. It may be profitable to illustrate these four types of response with brief case reports.

CASE REPORTS

CASE 5 (Table II) —A 32 year old soldier was injured by shell fragments on 1944, and was admitted to the Mayo General Hospital on September 1, with a large aneurysm in the region of the right femoral artery. There was no essential difference in color or temperature of the two feet. The reactive hyperemia test was carried out on several occasions between the date of admission and the latter part of October. No flush appeared in the foot during a period of three minutes, whereas a brilliant flush appeared immediately after release of pressure from the femoral artery. Lumber sympathectomy was performed on October 31. The reactive hyperemia test was carried out for the first time on the third postoperative day. The flush was almost instantaneous, reached the toes in five seconds, was complete and full in sixty seconds, and showed no further improvement upon release of pressure from the femoral artery. Excision of the femoral aneurysm on November 6, with concomitant ligation of the femoral vein, was followed by an excellent result, the foot maintaining at all times good warmth and color.

CASE 19 (Table II) —A 26 year old officer sustained an injury from a shell fragment on April 16, 1943, and was admitted to the Mayo General Hospital on May 29, with a mid femoral arteriovenous fistula. There was no flush of the foot during the reactive hyperemia test. Sympathectomy was performed on July 14. When tested again one week later, a flush appeared in some of the toes in fifteen seconds and it became complete and of good quality in two minutes. However, there was a much more brilliant flush when pressure was released from the femoral artery. By August 17 the reactive hyperemia test showed an excellent flush which began in the toes in ten seconds and was complete and full in eighty seconds without improvement upon release of pressure from the femoral artery. On August 20 the fistula and the involved area of artery and vein were excised and a vein graft was utilized to bridge the arterial defect. The graft was successful and the patient had excellent circulation in the limb.

CASE 5 (Table III) —A 20 year old soldier was injured on Dec 10, 1944, and was admitted to the Mayo General Hospital on March 7, 1945, with a fairly large popliteal aneurysm. There was a poor and incomplete flush during the reactive hyperemia test on admission and during the next few weeks. On April 19 sympathectomy was performed. The results of the test steadily improved. For example on May 3 a flush first reached the toes in thirty seconds. It improved slowly during the two minute period of observation but became strikingly better upon release of pressure from the popliteal artery. By July 30 the flush reached the toes in ten seconds. Although it improved considerably during the two minute period of observation, it improved still further upon release of pressure from the popliteal artery. The aneurysm was explored on August 3. The popliteal artery was occluded with a rubberband clamp just proximal to the aneurysm. The foot maintained good color and warmth. The sac was opened and the artery transfixed above and below the defect. After operation the foot was always warm and well colored.

CASE 7 (Table III) —A 27 year old soldier was injured on Feb 26, 1945, and was admitted to the Mayo General Hospital on May 4, with signs of femoral arteriovenous fistula. No flush occurred during the reactive hyperemia test on admission or during the ensuing weeks. Finally, on June 5, sympathectomy was performed. There was only slight improvement after this procedure, the flush being of poor quality and incomplete in extent. During the following weeks there was no noticeable change. Thinking that some local factor might be responsible for the poor reactive hyperemia test and that the collateral circulation might actually be adequate the lesion was cautiously explored on August 23. When a rubber band clamp was placed upon the artery above and below the fistula, the foot became extremely pale and cool and remained so as long as the clamps were left in place. The wound was closed without any attempt to extirpate the fistula. The limb was tested repeatedly during the next few months. Finally, on January 11, the vessels were again explored. Once more precise occlusion of the artery caused persistent pallor and coolness of the foot. The

tion In some the tests became definitely better but in none did they become adequate according to the standards which I feel should be followed as indicating reliably efficient collateral circulation.¹⁶ It will be noted that in these cases a longer interval elapsed between sympathectomy and operation upon the aneurysm or fistula than in those cases listed in Table II. In only a single instance was this interval less than five weeks and in nine or 64.3 per cent it was two months or longer. It will also be seen that in one patient a satisfactory cure by thrombosis occurred making operation unnecessary and that in nine patients the continuity of the affected artery was maintained or restored by ligation of the fistula by end-to-end suture or by vein transplant. In only four or 28.6 per cent was it necessary to ligate the involved artery. In all cases an excellent result was obtained. The limbs maintained good color and warmth and there was no sensitivity to cold. Nerve return progressed satisfactorily when a peripheral nerve paralysis had been present. In those cases in which the continuity of blood flow through the affected artery was successfully maintained there was in addition no fatigue on exercise unless such fatigue had been present before operation.

In all cases the color and warmth of the affected hand or foot was observed during a prolonged period of precise occlusion of the artery with a rubber shod clamp at the time of operation. In all instances save one this period of observation showed that the collateral circulation was actually adequate although repeated preoperative tests had led to a different interpretation. That the collateral circulation was efficient in at least the four instances in which the involved artery was ligated is evident from the postoperative result. In many of the cases some anatomic condition was found at the time of exploration which explained adequately the reason for the false results of the tests carried out before operation, for example the presence of some large collateral vessels which would necessarily have been occluded during digital compression but which could be preserved at operation.¹⁶ That the collateral circulation was apparently actually satisfactory in all save the one case referred to and probably the one case in which operation was unnecessary does not necessarily signify that it had been rendered so by sympathectomy. All that can be said is that the same tests for collateral circulation before and after sympathectomy showed some improvement in all instances after this procedure and great improvement in some but that they did not become completely satisfactory in any.

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CASE REPORTS

CASE 5 (Table II)—A 32 year old soldier was injured by shell fragments on 1944 and was admitted to the Mayo General Hospital on September 1, with a large aneurysm in the region of the right femoral artery. There was no essential difference in color or temperature of the two feet. The reactive hyperemia test was carried out on several occasions between the date of admission and the latter part of October. No flush appeared in the foot during a period of three minutes, whereas a brilliant flush appeared immediately after release of pressure from the femoral artery. Lumbar sympathectomy was performed on October 31. The reactive hyperemia test was carried out for the first time on the third postoperative day. The flush was almost instantaneous, reached the toes in five seconds, was complete and full in sixty seconds, and showed no further improvement upon release of pressure from the femoral artery. Excision of the femoral aneurysm on November 6, with concomitant ligation of the femoral vein, was followed by an excellent result, the foot maintaining at all times good warmth and color.

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CASE 6 (Table III)—A 20 year old soldier was injured on Dec 10, 1944, and was admitted to the Mayo General Hospital on March 7, 1945 with a fairly large popliteal aneurysm. There was a poor and incomplete flush during the reactive hyperemia test on admission and during the next few weeks. On April 19 sympathectomy was performed. The results of the test steadily improved. For example, on May 3 a flush first reached the toes in thirty seconds. It improved slowly during the two minute period of observation but became strikingly better upon release of pressure from the popliteal artery. By July 30 the flush reached the toes in ten seconds. Although it improved considerably during the two minute period of observation, it improved still further upon release of pressure from the popliteal artery. The aneurysm was explored on August 3. The popliteal artery was occluded with a rubberband clamp just proximal to the aneurysm. The foot maintained good color and warmth. The sac was opened and the artery transected above and below the defect. After operation the foot was always warm and well colored.

CASE 7 (Table III)—A 27 year old soldier was injured on Feb 26, 1945, and was admitted to the Mayo General Hospital on May 4 with signs of femoral arteriovenous fistula. No flush occurred during the reactive hyperemia test on admission or during the ensuing weeks. Finally on June 5, sympathectomy was performed. There was only slight improvement after this procedure, the flush being of poor quality and incomplete in extent. During the following weeks there was no noticeable change. Thinking that some local factor might be responsible for the poor reactive hyperemia test and that the collateral circulation might actually be adequate, the lesion was cautiously explored on August 25. When a rubber band clamp was placed upon the artery above and below the fistula, the foot became extremely pale and cool and remained so as long as the clamps were left in place. The wound was closed without any attempt to extirpate the fistula. The limb was tested repeatedly during the next few months. Finally, on January 11, the vessels were again explored. Once more precise occlusion of the artery caused persistent pallor and coolness of the foot. The

fistula was carefully dissected out, and it became evident that it could be transferred and reinforced by a segment of the divided vein with preservation of the continuity of the artery. This was done with excellent result.

TABLE IV. SYMPATHECTOMY PERFORMED BEFORE OPERATION FOR ANEURYSM OF FISTULA INDICATION—IMPOSSIBILITY OF TESTING THE COLLATERAL CIRCULATION

CASE NO.	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPATHECTOMY (IN MO.)	INTERVAL BETWEEN SYMPATHECTOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Arterial Aneurysm</i>						
1	Innominate	9	6	Triplication	At previous exploration hand became completely paralyzed with innominate occlusion partial proximal ligation had failed as judged by oscillometer, etc.	Excellent
2	Subclavian	4.5	2	A E	Also plexus injury requiring lysis	Excellent
3	Axillary	2.5	7	A E	Also plexus injury requiring lysis also cold sensitivity	Good cold sensitivity
4	Axillary	3	2	A E	Also plexus injury requiring lysis	Excellent
5	Femoral	1.5	2.5	A	Huge aneurysm edema coldness of foot pain circulation and pain improved after sympathectomy	Excellent
6	Popliteal	2	1	A	Huge infected aneurysm, loss anterior tibial group muscles large ulcer, aneurysm ruptured subcutaneously 5 days after sympathectomy forcing operation	Excellent
<i>Cases of Arteriovenous Fistula</i>						
7	Aorta innominate subclavian	5.5	10	Exploration	Thought before exploration to involve innominate vessels	—
8	Subclavian	8.5	2	E	An intramediastinal fistula	Excellent
9	Subclavian	4.5	2	Exploration	Continuous bruit and thrill disappeared after sympathectomy slight systolic bruit remained	Excellent thrombosis of fistula
10	Brachial	2	1	E	Huge A V vascular aneurysm pain and swelling prohibited testing collateral severe plexus injury requiring lysis and restore circulation of hand impaired cold sensitivity rupture 3 days after sympathectomy forced operation	Good slight cold sensitivity

SYMPATHECTOMY PERFORMED BECAUSE OF IMPOSSIBILITY OF TESTING THE COLLATERAL CIRCULATION

Table IV summarizes data concerning ten patients in whom sympathectomy was performed because it was impossible to compress the involved artery at the site of the aneurysm or fistula and consequently to test the state of

the collateral circulation. In three cases the artery could not be compressed near the affected portion because of the very large size of the aneurysm and the great pain associated with it. In four cases the lesion was within the mediastinum. In the other three cases axillary or subclavian lesions were so covered by the clavicle and the heavy musculature that the artery could not be occluded near the site of the defect. Since in these cases with one exception there is no way in which one can tell what the result might have been had sympathectomy not been performed it is difficult to evaluate the effect of this procedure. Certain data are suggestive however that sympathectomy was beneficial. In the first place in the exceptional case mentioned previously (Case 1) complete pallor had occurred during temporary occlusion of the innominate artery proximal to the aneurysm during an exploratory mediastinotomy. A partial proximal ligation was done but the resulting reduction in pulsation and oscillometry in the extremity was so transient that it was obvious that the proximal ligation was a failure. Complete proximal and distal ligation after sympathectomy resulted in cure of the aneurysm and the maintenance of excellent circulation in the hand. In two patients (Cases 3 and 10) some sensitivity to cold was present after operation. Judging from the beneficial effects of sympathectomy in improving or relieving cold sensitivity following ligation of arteries for the cure of aneurysm or fistula²³ there is every reason to suppose that these patients would have had more annoying sensitivity to cold had sympathectomy not been performed. Two patients (Cases 5 and 10) who had severe pain were more comfortable after sympathectomy than before. In the four patients (Cases 2, 3, 4 and 10) in whom there was extensive damage to the brachial plexus return of nerve function has been as good as could reasonably be expected considering the state of the nerves at the time of exploration. In one patient (Case 9) signs of a mediastinal subclavian fistula disappeared after sympathectomy. The possible role of sympathetic denervation in bringing about cure through thrombosis will be discussed subsequently. Obviously the sympathectomy performed in Case 7 in which the vascular lesion was afterward found inoperable was seen in retrospect to have been needless.

SYMPATHECTOMY PERFORMED BECAUSE OF VASOSPASM

In Table V are recorded data upon six patients in whom sympathectomy was performed primarily because of vasospasm. In three of them there was evidence of intense persistent vasospasm in the affected limb. In the other three patients there was in addition a long standing history of a pronounced tendency to vasospasm in all the extremities. Since maintenance of adequate circulation would depend upon full utilization of the existing collateral vessels should operative cure necessitate ligation of the affected main artery it is important that this circulation not be compromised by persistent vasoconstriction. The only means of being certain that such vasoconstriction will not jeopardize the circulation is by interruption of the sympathetic innervation. The results in these cases and in a number of others listed in other tables in which definite vasospasm was present suggest that sympathectomy yields excellent results in such cases. In all of them the hand or foot remained warm and well

TABLE V SYMPATHECTOMY PERFORMED BEFORE OPERATION FOR ANEURYSM OR FISTULA, INDICATION—VASOSPASM

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPATHECTOMY (IN MO)	INTERVAL BETWEEN SYMPATHECTOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Intertor Aneurysm</i>						
1	Femoral	3.5	2	E	Mal foot amputation had been done for trauma large ulcer, rapid healing after sympathectomy	Excellent healed cave suit able for Syme am putation
<i>Cases of Arterovenous Fistula</i>						
2	Femoral	7	4.5	E	Long history of vasospasm tests for collateral circulation only fair before good after sympathectomy	Excellent
3	Femoral	3	7	F	Long history Raynaud like disorder	Excellent
4	Popliteal	2.5	7	E	Marked vasospasm for years tests for collateral circulation only fair before sympathectomy	Excellent
5	Popliteal	3	1	F	Affected foot remained cold in ordinary room temperature other warm ulcer of leg	Excellent
6	Foot arterial		4	E	Cyanosis and coldness of foot had followed excision of posterior tibial A V, two A V's remained to be excised involving peroneal and anterior tibial vessels one excised at time of sympathectomy other 4 weeks later, cyanosis and coldness disappeared after sympathectomy	Good only difficulty was slow healing of ulcer of foot

colored after operative cure of the aneurysm or fistula. In several of the patients in whom tests for collateral circulation were only fair before sympathectomy, these tests became good following the procedure.

SYMPATHECTOMY PERFORMED BECAUSE OF CAUSALGIA, ISCHEMIC LESIONS AND OTHER CONDITIONS

Table VI includes seven patients for whom sympathectomy was performed because of various indications. In two (Cases 2 and 3) the procedure was carried out chiefly because of causalgia. Prompt and complete relief occurred in Case 2. In Case 3 the patient felt about 90 per cent relieved and was addicted to morphine. In Case 4 the patient was unable to walk because of pain in the metatarsals which were badly shattered. The entire foot was extensively infected.

TABLE VI SYMPATHECTOMY PERFORMED BEFORE OPERATION FOR ANEURYSM OR FISTULA, MISCELLANEOUS INDICATIONS

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPATHECTOMY (IN MO)	INTERVAL BETWEEN SYMPATHECTOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Arterial Aneurysm</i>						
1	Axillary	8	2	E	Impaired circulation extensive plexus injury requiring lysis and radial suture	Excellent
2	Axillary	2	12	E	Causalgia relief after sympathectomy	Excellent
<i>Cases of Arteriovenous Fistula</i>						
3	Femoral	1	15	E	Causalgia superficial gangrene of toe and foot peroneal palsy FCC femur pain relieved ulcers healed slowly after sympathectomy	Excellent
4	Femoral	2	16	E	Gangrene of toes multiple fractures of metacarpals compound and infected FCC femur healing after sympathectomy and amputation of toes fractures healed infection cleared	Excellent
5	Femoral	5	25	E	Impaired circulation and complete sciatic paralysis nerve suture had been done ulcer of foot	Good ulcer healed some cold sensitivity
6	Popliteal	2	7	E	Peroneal paralysis collateral circulation only fair before sympathectomy	Excellent
7	Ulnar circ d		1	E		-
<i>Excision in a radical excision</i>						

infected and there was a compound comminuted fracture of the femur. The gangrenous toes were amputated at the time of sympathectomy. The end result was cure of the fistula, healing of the fractures, clearing of the infection and a useful limb with excellent circulation. Three patients (Cases 1, 5, and 6) had peripheral nerve lesions in limbs in which the circulation was obviously impaired or in which the collateral circulation was judged to be only questionably adequate. In addition one had an ulcer of the foot. The remaining patient (Case 7) was one in whom three previous attempts by other surgeons had failed to effect a cure and in whom both the ulnar and radial arteries had been ligated and divided. It seemed likely that important collateral vessels

in the hand against ischemic difficulties. Operative cure necessitated excision of the flexor sublimis muscle and the extensive vascular channels in and about this muscle. Circulation in the hand remained excellent.

SYMPATHECTOMY PERFORMED NEEDLESSLY BECAUSE OF ERROR
IN LOCALIZING THE LESION

In Table VII are summarized seven cases in which sympathectomy was performed because an aneurysm or fistula was thought preoperatively to involve arteries other than those actually affected and in which tests, as well as they could be carried out, indicated poor collateral circulation. In three cases (Cases 1, 2, and 3) digital pressure sufficient to still the aneurysm or fistula invariably occluded the overlying femoral as well as the involved profunda femoral artery. In all of them it was thought, consequently, that the lesion was of the femoral or common femoral artery. In Cases 4 and 5 the fistula was in such close proximity to the popliteal artery that the bruit and thrill could be eliminated only by digital pressure which compressed the adjacent popliteal artery. In

TABLE VII SYMPATHECTOMY PERFORMED BEFORE OPERATION FOR ANEURYSM OR FISTULA
CASES IN WHICH A MISTAKE IN LOCALIZATION OF THE LESION WAS MADE

CASE NO	PREOPERATIVE LOCALIZATION	ACTUAL LOCATION OF LESION	INTERVAL BETWEEN INJURY AND SYMPATHECTOMY (IN MO)	INTERVAL BETWEEN SYMPATHECTOMY AND OPERATION (IN WEEKS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Arterial Aneurysm</i>							
1	Femoral	Profunda	3	10	A	Compression which stills aneurysm obliterated femoral pulse thrombosis and shrinkage occurred after sympathectomy but not persisted	Excellent
<i>Cases of Arteriovenous Fistula</i>							
2	Common femoral	Profunda	23	10	E	Compression which eliminated bruit and thrill stopped femoral pulse	Excellent
3	Femoral	Profunda	6	8	E	Compression which eliminated bruit and thrill stopped femoral pulse	Excellent
4	Popliteal	Gonoculate	8	6	E	Bruit and thrill could not be eliminated by pressure without loss of popliteal pulse	Excellent
5	Popliteal	Posterior tibial	5	6	E	A very high posterior tibial lesion; bruit and thrill could not be eliminated by pressure without loss of posterior and anterior tibial pulse	Excellent
6	Subclavian	Transverse cervical	45	3	E	Bruit and thrill could not be stopped by pressure without loss of brachial pulse	Excellent
7	Posterior and anterior tibial	Posterior tibial	35	4	E	Bruit and thrill could be stopped only by pressure which caused loss of anterior and posterior tibial pulses; had tibial paralysis and FFC fibula	Excellent

Case 6 a fistula between the transverse cervical artery and the internal jugular vein could be occluded only by pressure which obliterated the brachial pulse and was thought to involve the subclavian vessels. In the remaining case an instance of a posterior tibial fistula it was feared that the anterior tibial vessels might also be involved since the fistula could be closed only by compression which occluded the anterior as well as the posterior tibial artery. Perhaps the extensive fracture of the fibula contributed to the difficulty of accurate digital compression. In all cases tests for collateral circulation were poor before and good after sympathectomy. It is apparent in retrospect that had correct localization been possible sympathectomy could have been safely omitted. It is also apparent in retrospect that in all cases except possibly Case 4 arteriograms might have established the correct location of the lesion.

SYMPATHECTOMY PERFORMED AT TIME OF OPERATION UPON ANEURYSM OR FISTULA

In nine instances sympathectomy and operative attack upon the aneurysm or fistula were performed at the same session. The cases are summarized in Table VIII. In one patient (Case 9) sympathectomy was carried out primarily because the sympathetic chain was easily exposed in the operative incision through which the iliac artery had been isolated as a preliminary safeguard. The fistula was so high that it was thought to involve the common femoral vessels. Actually there was a fistula between the medial circumflex femoral artery and the common femoral vein. In another instance (Case 5) sympathectomy might also have been omitted had the fistula been correctly localized before exploration. This patient had a very large aneurysm in the anterior aspect of the thigh which could be stilled only by pressure which occluded the femoral artery. The profunda had been previously ligated shortly after injury. Tests for collateral circulation were extremely poor before and excellent after sympathectomy. In reality the aneurysm involved only the lateral femoral circumflex artery. The results were excellent in all cases but two. In one (Case 7) although the foot at all times after operation was warm and well colored some peroneal sensory loss without motor involvement was added to the pre-existing tibial and saphenous anesthesia. Because at no time was there evidence of circulatory impairment it seems more likely that this complication was due to pressure from the tourniquet than to postoperative ischemia. In the other patient (Case 3) chemic paralysis developed after operation from which he fortunately made a complete recovery. The circulation was obviously impaired for a few hours after operation although the limb rapidly regained and maintained normal warmth and color. This was a case in which sympathectomy and operation upon the vascular lesion were performed concomitantly without retesting the collateral circulation following sympathectomy—an omission which we have learned to avoid. That it is sometimes advantageous to do both operations at one sitting is obvious from consideration of those cases in which severe pain was present. In Case 2 for example a very large popliteal aneurysm which had ruptured subcutaneously was so painful that the patient was writhing in agony and large doses of morphine were ineffective in affording relief. The reactive hyperemia test was characterized by complete absence of

TABLE VIII SYMPATHECTOMY PERFORMED AT THE TIME OF OPERATION FOR ANEURYSM OF FISTULA

NO CASE	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND OPERATION (IN DAYS)	TYPE OF OPERATION	COMMENT	RESULT
<i>Cases of Arterial Aneurysm</i>					
1	Popliteal	3	A	Infected, subcutaneously ruptured aneurysm with severe pain	Excellent
2	Popliteal	3	A	"	" excellent
3	Popliteal	6	E	"	hemie palsy developed re-
4	Popliteal	4	A	"	entry
5	Lateral femoral circum flex	11	A	and much pain reactive hyperemia test excellent after sympathectomy Profundus had been ligated at time of injury, aneurysm could be stifled only by pressure which stopped femoral pulse, reactive hyperemia test nil before sympathectomy, good flush 30 seconds after sympathectomy	provement in ischemic palsy Excellent
<i>Cases of Arteriovenous Fistula</i>					
6	Common femoral	4.5	E	Tests for collateral circulation poor before operation	Excellent
7	Femoral	3	E	Large painful subcutaneously ruptured aneurysm tibial and peroneal sensory loss previously poor tests for collateral circulation became good after sympathectomy	Foot remained warm, well colored, some peroneal sensory loss perhaps due to tourniquet
8	Hipogastric	5	E	External iliac fistula on same side had been exercised 7 weeks after injury tests for collateral circulation poor before, good after sympathectomy	Excellent
9	Medial circum flex femoral	13	E	It was caused by surgical ligation of the femoral artery at time of injury brunt and thrill could be stopped only by high pressure in femoral area iliac arteries explored as precautionary measure sympathectomy done only because chain lay exposed during procedure	Excellent

flush Following sympathectomy a complete and intense flush was present within thirty seconds after release of the constricting cuff Aneurysmorrhaphy was promptly done The patient was entirely comfortable after operation and the foot had excellent circulation

EFFECT OF SYMPATHECTOMY UPON EXERCISE TOLERANCE AND COLD SENSITIVITY

There remains to be considered the influence of sympathectomy upon the two commonest functional disorders which follow the ligation of arteries for

the cure of aneurysms and fistulas namely decrease in exercise tolerance and sensitivity of the limb to cold. In regard to the effect of sympathectomy upon intermittent claudication or its equivalent it will be best to consider only those vascular lesions involving the popliteal femoral and common femoral arteries since reduction in exercise tolerance is particularly noticeable after ligation of these vessels. It is necessary to eliminate those cases in which walking was made difficult because of associated fractures amputation or motor loss from peripheral nerve injury. It is also necessary to exclude those few cases in which the walking distance was apparently significantly reduced before operation at a time when the continuity of blood flow through the affected artery was uninterrupted. In addition those cases must be excluded in which it was possible to preserve the continuity of the artery at the time of operation. Exercise tolerance was determined by having the patient walk at normal pace with a pedometer or over a measured course until he was forced to stop because of fatigue or more rarely cramps in the limb. The distance was approximately the same in the two groups. Those whose operation had necessitated ligation of the popliteal artery were forced to stop after walking an average of 0.68 miles in the group who had not undergone sympathectomy 0.73 miles in the other group. The distance was the same an average of 0.73 miles in the sympathectomized and control groups of patients whose operation had necessitated ligation of the femoral or common femoral artery.

These data demonstrate that exercise tolerance was almost precisely the same regardless of whether sympathectomy had been performed. Unfortunately the two groups are not carefully controlled from several important standpoints. The interval between operation and final testing of walking distance varied from patient to patient. Consideration of this factor is furthermore futile because some patients rapidly reached their apparent maximal exercise tolerance whereas others noted slow and more prolonged improvement in the distance they could walk. In addition one cannot analyze properly the possible exaggeration of this symptom on the part of some patients in a desire to avoid duty and to be separated from the service. Finally the two groups are not entirely comparable in that there was evidence from various tests and observations that the collateral circulation was more efficient in the group in which sympathectomy was considered unnecessary.

In regard to the effect of sympathectomy in preventing sensitivity of the limb to cold analysis of the cases gives more clear cut information. Sensitivity to cold of varying degree followed operation upon the subclavian axillary and brachial arteries in which ligation was necessary or reparative procedures failed to maintain continuity of the vessel in 5 of 18 patients (27.2 per cent) in whom sympathectomy was performed before or at the time I operated and in only one of 32 cases (3.1 per cent) of popliteal femoral or common femoral lesions treated similarly. Of these 6 patients cold sensitivity was present before operation in 2. On the other hand cold sensitivity was present after operation in 13 of 42 (31 per cent) patients treated for lesions of the subclavian axillary and brachial vessels without sympathectomy and in 5 of the 65 (7.7 per cent) cases with popliteal femoral or common femoral lesions. Eight of

these 18 patients had some cold sensitivity before operation. Among those patients operated upon elsewhere sensitivity to cold was present in 5 of 11 (45 per cent) with aneurysms or fistulas of the main arteries to the upper extremity and in 9 of 30 (30 per cent) with lesions of the main arteries of the lower extremities. The single patient who had been sympathectomized at the time of operation had no cold sensitivity. Altogether 13.7 per cent of those 31 patients sympathectomized before operation upon the vascular lesions under consideration had sensitivity of the limb to cold and 21.6 per cent of those 142 patients who did not undergo sympathectomy.

EFFECT OF SYMPATHECTOMY UPON INTRASACULAR THROMBOSIS

Not uncommonly sympathectomy was followed by a noticeable increase in the mural thrombus within the aneurysmal sac. Sometimes this process was very extensive. For example in one patient (Case 1 Table VII) a large pulsating aneurysm in the thigh became after sympathectomy progressively smaller and firmer and eventually lost its pulsation. Indeed clinically it appeared that the sac had been obliterated. Arteriograms however revealed the persistence of a sac several centimeters in diameter. At operation the laminated mural thrombus was many times larger than the remaining aneurysmal cavity. In two instances apparent cures occurred. In one (Case 9 Table IV) there were signs suggestive of an arteriovenous fistula of the proximal portion of the left subclavian vessels. After sympathectomy the thrill and continuous bruit disappeared and only a short systolic bruit remained. In the belief that a saccular aneurysm remained the extramediastinal portions of the vessels were explored. No aneurysm was encountered and there was such dense scarring about the vessels as one approached the mediastinum that exploration was discontinued on the assumption that the remaining systolic bruit was probably the result of partial compression of the artery by scar tissue. The other patient (Case 3 Table III) had a pulsating femoral aneurysm about 7 cm. in diameter and evidence of completely inadequate collateral circulation. Sympathectomy was performed two months after injury. After this procedure the aneurysm became steadily a little firmer and smaller and pulsated less vigorously. This process was slow during the first few months but finally six months after sympathectomy only a small firm nonexpansile mass remained. Arteriograms revealed almost complete obliteration of the sac. During the ensuing few weeks the mass practically disappeared and it was evident that a satisfactory cure had been obtained.

It must be pointed out that spontaneous cure occurs occasionally without sympathectomy in cases of both arterial aneurysm and arteriovenous fistula. Indeed this occurred in 11 of 22 cases studied in incidence of 49 per cent. On the other hand a cure by thrombosis occurred in only 2 of 78 patients sympathectomized an incidence of 2.6 per cent. It is therefore difficult to be certain that the thrombosis is actually the result of the sympathectomy. This is particularly true when complete thrombosis occurs gradually and over a long period of time as in Case 3 Table III. When it occurs promptly after sympathectomy as in some of the cases recorded in the literature the march of

events would suggest that this process has resulted from sympathectomy. This seems all the more likely because of incomplete thrombosis of the sac which is commonly observed after sympathetic denervation. Gage suggested that the responsible mechanism was the decrease in peripheral resistance. I know of no better hypothesis.

The question arises whether the increase in mural thrombus or the complete thrombosis of the sac can be associated with extension distally of the clot. The course of one patient (Case 9, Table II) suggests that, rare as it may be, this occurrence may take place. The patient was a 49 year old man with an arteriosclerotic aneurysm of the popliteal artery. On admission to the hospital there was a right popliteal aneurysm which pulsated vigorously and had a loud systolic bruit. There was evidence of peripheral arteriosclerosis. The right dorsal pedal pulse was present, the posterior tibial absent, both were present in the left foot. Collateral circulation was very poor. These findings were checked the day before sympathectomy, but unfortunately the pulses were not palpated and oscillometric studies were not made immediately before sympathectomy. The day after sympathectomy the aneurysm was noted to be somewhat firmer and to have only a faint shoe-like sound in place of the systolic bruit. The dorsal pedal pulse had disappeared and oscillometric studies confirmed the impression that the popliteal artery was occluded distal to the aneurysm. This, as well as the recent increase in the extent of mural thrombus, was substantiated at operation eight days later. Although there is no proof in this case, the evidence suggests that the extension of the mural thrombus following sympathectomy brought about occlusion of the artery distal to the aneurysm. An excellent result followed aneurysmorrhaphy.

DISCUSSION

In considering the role of sympathectomy in the operative treatment of aneurysms and arteriovenous fistulas it is important to keep in mind that, in the hands of those familiar with it, this procedure is associated with very little discomfort and minimal risk. Patients can be ambulatory the day after either dorsal or lumbar sympathectomy. In my own experience there have been no deaths and complications have been extremely rare. In these cases I have preferred abolishing vasoconstrictor impulses by operative sympathectomy rather than by injection of alcohol, for two reasons: permanence of the sympathetic denervation, and absence of the neuritic pains which sometimes are a distressing sequel of alcohol injection.

The series of cases presented gives convincing evidence of the fullness of the circulation in the extremities after sympathectomy. The maintenance of excellent warmth and color in the sympathectomized hand or foot in cases in which cure of the vascular lesion had entailed arterial ligation and more particularly by the striking improvement in the tests for collateral circulation which so often occurs immediately after sympathectomy has been carried out. I do not feel that these data offered convincing proof that sympathectomy actually increases the collateral circulation by foster-

these 18 patients had some cold sensitivity before operation. Among those patients operated upon elsewhere sensitivity to cold was present in 5 of 11 (45 per cent) with aneurysms or fistulas of the main arteries to the upper extremity and in 9 of 30 (30 per cent) with lesions of the main arteries of the lower extremities. The single patient who had been sympathectomized at the time of operation had no cold sensitivity. Altogether 13.7 per cent of those 51 patients sympathectomized before operation upon the vascular lesions under consideration had sensitivity of the limb to cold and 21.6 per cent of those 14 patients who did not undergo sympathectomy.

EFFECT OF SYMPATHECTOMY UPON INTRASACULAR THROMBOSIS

Not uncommonly sympathectomy was followed by a noticeable increase in the mural thrombus within the aneurysmal sac. Sometimes this process was very extensive. For example in one patient (Case 1 Table VII) a large pulsating aneurysm in the thigh became after sympathectomy progressively smaller and firmer and eventually lost its pulsation. Indeed clinically it appeared that the sac had been obliterated. Arteriograms however revealed the persistence of a sac several centimeters in diameter. At operation the laminated mural thrombus was many times larger than the remaining aneurysmal cavity. In two instances apparent cures occurred. In one (Case 9 Table IV) there were signs suggestive of an arteriovenous fistula of the proximal portion of the left subclavian vessels. After sympathectomy the thrill and continuous bruit disappeared and only a short systolic bruit remained. In the belief that a sacular aneurysm remained the extramedastinal portions of the vessels were explored. No aneurysm was encountered and there was such dense scar ring about the vessels as one approached the mediastinum that exploration was discontinued on the assumption that the remaining systolic bruit was probably the result of partial compression of the artery by scar tissue. The other patient (Case 3 Table III) had a pulsating femoral aneurysm about 7 cm. in diameter and evidence of completely inadequate collateral circulation. Sympathectomy was performed two months after injury. After this procedure the aneurysm became steadily a little firmer and smaller and pulsated less vigorously. This process was slow during the first few months but finally six months after sympathectomy only a small firm nonexpansile mass remained. Arteriograms revealed almost complete obliteration of the sac. During the ensuing few weeks the mass practically disappeared and it was evident that a satisfactory 'cure' had been obtained.

It must be pointed out that spontaneous cure occurs occasionally without sympathectomy in cases of both arterial aneurysm and arteriovenous fistula. Indeed this occurred in 11 of 225 cases studied in incidence of 4.9 per cent. On the other hand a cure by thrombosis occurred in only 2 of 78 patients sympathectomized an incidence of 2.6 per cent. It is therefore difficult to be certain that the thrombosis is actually the result of the sympathectomy. This is particularly true when complete thrombosis occurs gradually and over a long period of time as in Case 3 Table III. When it occurs promptly after sympathectomy, as in some of the cases recorded in the literature the march of

involved artery once operation is attempted sympathectomy appears to me as the wiser procedure. In the majority of cases in this series in which sympathectomy was carried out because of poor tests for collateral circulation these tests became satisfactory fairly promptly. Even in those difficult cases in which the tests did not become adequate the procedure gave one some definite satisfaction in the knowledge that vasoconstriction had been eliminated.

Where the aneurysm or fistula is associated with a peripheral nerve lesion which requires operative treatment and where the collateral circulation is precarious the indication for sympathectomy seems clear cut. It is imperative that the nerve lesion be treated early rather than late and it is too hazardous to attempt nerve repair before operative cure of the aneurysm or fistula. Any effort to improve the collateral circulation so as to permit early operative treatment is worth while. Similarly sympathectomy seems advisable when such vascular and nerve lesions are associated with obvious evidence of impaired circulation in the extremity regardless of whether the collateral circulation appears to be adequate or inadequate. In such cases one must presume that operative cure will necessitate ligation of the artery and further reduction in circulation to the limb and it seems apparent that a good vascular supply fosters nerve regeneration just as impaired circulation may produce ischemic nerve injury. My data are insufficient for quantitative comparison of nerve regeneration in patients with nerve injuries with unimpaired circulation and in those with ligated arteries in limbs which have been sympathectomized but they give one the impression that nerve restoration is comparable in the two groups. The data do offer conclusive proof that sympathectomy may be of great benefit in cases of ischemic nerve injury with impaired circulation resulting from arterial ligation division or thrombosis a subject which will be presented in another communication.

Sympathectomy may be advisable in certain cases in which the anatomic location of the aneurysm or fistula prevents digital occlusion of the artery and in which the artery affected is one of those the ligation of which is sometimes followed by ischemic troubles. When the artery cannot be compressed precisely at the site of its defect one can sometimes compress it proximally or distally and obtain some notion of the state of the collateral circulation. It must be kept in mind however that such tests may give erroneous results either through the occlusion of collateral channels which can be preserved during operative attack upon the lesion or through nonocclusion of channels which may have to be sacrificed.

Where ischemic lesions are present distal to an aneurysm or fistula sympathectomy is entirely rational. Cure of the aneurysm or fistula may entail ligation of the artery and still further reduction in circulation. Even if the blood flow through the artery can be preserved there is every need for increasing the circulation which is obviously insufficient as evidenced by the ischemic lesion present.

If the main artery to a limb must be ligated in the cure of the vascular lesion one can ill afford the risk of having the circulation jeopardized by vasospasm in the collaterals. It must be pointed out that vasospasm is not

ing growth of new collateral channels. Certainly those cases in which the collateral circulation shows only slight improvement immediately after sympathectomy but steady significant improvement during ensuing weeks and months would suggest that sympathectomy may have this effect. It must be pointed out, however, that a number of cases have been observed in which without any effort to increase the collateral circulation the formerly poor tests have shown a remarkable improvement during a short period of observation. Consequently it is my feeling that the observations cited are somewhat suggestive but certainly offer no proof that sympathectomy actually promotes the growth of new collaterals.

The immediate effect of sympathectomy upon the state of collateral circulation can be predicted with reasonable accuracy by comparing the results of the reactive hyperemia test in any given patient under ordinary environmental conditions and those obtained during reflex vasodilatation or anesthesia or better still during procaine sympathetic block. I think however, that such studies are unnecessary as a routine measure and that one can proceed with sympathectomy where the indications are plain. Should tests for collateral circulation during such preoperative studies show a distinct improvement one would have only additional confirmation of the advisability of sympathectomy. Should these tests show no improvement the state of the circulation would be sufficiently precarious to warrant the use of any reasonably safe procedure to add some safeguard against ischemic difficulties.

The results of sympathectomy and a rational outline for its use in cases of aneurysm or fistula can best be evaluated by a brief review of the various indications for its use. In the first place it seems advisable to employ the procedure in cases where there is evidence of poor collateral circulation in which the lesions are of sufficient duration to have ordinarily produced good collateral circulation and in which simpler means of improving the collateral circulation have shown no effect during a short period of trial. The literature is full of statements concerning the efficacy of intermittent proximal occlusion of the affected artery in improving the collateral circulation. In some cases the evidence that such an effect is being achieved is obvious¹⁴ but in many cases it is difficult to see any beneficial result. It would be a significant contribution to the problem of the treatment of aneurysms and fistulas if some controlled experimental and preferably clinical studies should establish beyond question the value and the limitations as well as the criteria for continuing or abandoning such procedures. With the present state of knowledge it is my belief that sympathectomy is indicated if no definite improvement in the tests for collateral circulation follows such efforts carried out during a period of some weeks. It is well established that permanent partial occlusion of the proximal artery is sometimes helpful in increasing the collateral circulation in cases of arterial aneurysm. This procedure is not applicable in instances of arteriovenous fistula.

Since sympathectomy in cases of aneurysm is as simple as partial proximal ligation and probably safer and since partial proximal ligation may jeopardize the chance of successfully maintaining or re-establishing the continuity of the

thrill of a fistula generally compresses the overlying femoral artery. As mentioned previously, arteriograms should ordinarily permit one to establish the correct localization in such cases.

It is also undoubtedly true that patients will be treated in whom operative cure of the aneurysm or fistula might have been accomplished without preliminary sympathectomy and without the occurrence of gangrene or ischemic paralysis. Where such serious complications appear to offer a definite threat it seems wise however to take every precaution to avoid them. One cannot afford to gamble with the viability of a patient's arm or leg. Indeed as the reported series of cases illustrates such disasters may occur even if sympathectomy is performed and it should be emphasized that the procedure offers no guarantee that some ischemic difficulty may not occur after ligation of an important artery. The utmost care in testing the collateral circulation and in avoiding injury to collateral vessels at the time of operation must be exercised or else the use of sympathectomy is doomed to be associated at times with disastrous results. The procedure must be looked upon as an aid in but not as a sure preventive of ischemic troubles.

In assaying the worth of sympathectomy two additional problems must be considered namely its effect upon fatigue on exercise and upon sensitivity to cold in limbs in which operative cure of aneurysm or fistula has necessitated ligation of an important artery. These are the commonest important symptoms in limbs in which otherwise adequate circulation has been maintained. Unfortunately analysis of this problem is difficult. Some idea can be obtained however by comparing the exercise tolerance before onset of fatigue of patients who had operations requiring ligation of the femoral or popliteal artery without preliminary sympathectomy and those with sympathectomy and by comparing the incidence of cold sensitivity in patients with and without sympathectomy who had ligations of the axillary brachial femoral or popliteal arteries. There was no essential difference in exercise tolerance in this series whether sympathectomy was performed or omitted. It has been pointed out that the two groups cannot be controlled properly in certain important regards. As will be discussed in another paper¹³ most of those patients in whom sympathectomy was performed after operative cure of aneurysm or fistula had only slight increase in exercise tolerance after this procedure or none at all although striking improvement was noted in some. One can form no well founded conclusions in regard to this problem but one gets the impression that sympathectomy rarely has any marked beneficial effect upon exercise tolerance. Although cold sensitivity occurs sometimes after ligation of arteries in the treatment of aneurysms and fistulas in patients who have had sympathectomy such disorders are more common and more severe in those in whom sympathectomy has not been carried out.

In his original publications Gage⁴ called attention to the frequent occurrence following sympathetic denervation of extensive thrombosis within the sac of the aneurysm. DeBakey¹⁷ had one case of a fistula of the carotid cavernous sinus in which cure by thrombosis took place after sympathectomy. Colson and Giddy¹⁸ performed lumbar sympathectomy in preparation for exploration

present in every limb in which a main arterial stem is ligated. Indeed, the vascular tone after such ligations may be high, low or normal. In some cases the limb actually exhibits evidence of vasodilatation and increased stability of skin temperature under varying environmental circumstances suggesting the effect of periarterial sympathetic interruption consequent to ligation and division of the artery. Where there is previous evidence of pronounced vasospasm it appears unwise however, to take any risk regarding its possible occurrence after operation. Such cases might be handled in two ways. One might proceed with operation and if alarming vasospasm ensues attempt to control it by sympathetic blocks or, if necessary, by sympathectomy. One might on the other hand prefer to take no risk and to perform sympathectomy either before the other operation or at the same time, if the tests for collateral circulation are good. The latter seems to me the safer method and hence is recommended in selected cases where there is intense vasospasm.

Sympathectomy may be required in the occasional case in which one or more of the main arteries to a limb have already been occluded by previous injury or operation and in which cure of an aneurysm or fistula may require ligation of other arteries essential to nutrition and proper function. Similarly an occasional case will be encountered in which an aneurysm or fistula is associated with severe cruralgia which can be temporarily relieved although not cured by sympathetic blocks.

Sympathectomy and the operation for cure of the aneurysm or fistula need not always be performed as separate procedures but can often be carried out at the same time. This can undoubtedly be done more often than it was in the present series of cases. Unless one has good evidence of unquestionably adequate collateral circulation beforehand one should under these circumstances always test the collateral circulation immediately after sympathectomy is accomplished and proceed with or abandon operative attack upon the aneurysm or fistula according to the results of such tests.

In all cases in which some specific indication for its use does not exist there appears to be no point in performing sympathectomy. If the indications already described are observed as a basis for the use of sympathectomy one will undoubtedly carry out the procedure sometimes when in retrospect it is seen that it might have been safely omitted. This will occur chiefly in those cases in which one will find it possible to maintain the continuity of blood flow through the affected artery by some reparative procedure. Since the feasibility of carrying out such procedures cannot be foreseen and since one cannot rely upon successful maintenance of blood flow in every instance in which they are attempted it is the part of wisdom to make as certain as possible that the collateral circulation is adequate before attempting extirpation of any aneurysm or fistula. If such practice means the performance of an occasional unnecessary sympathectomy, it is nevertheless wise. Sympathectomy will also be done needlessly if an aneurysm or fistula is improperly localized. Fortunately there is seldom any difficulty in localizing accurately the site of the lesion. Difficulty

SYMPATHECTOMY AS AN ADJUVANT IN THE OPERATIVE TREATMENT OF ANEURYSMS AND ARTERIOVENOUS FISTULAS

II SYMPATHECTOMY PERFORMED AFTER OPERATION

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THE role of sympathectomy as a preliminary to operations for the cure of aneurysm or arteriovenous fistula has been discussed elsewhere.¹ The usefulness of this procedure in increasing the efficacy of the collateral circulation in providing the limbs with the maximal or near maximal circulation possible in influencing favorably existing ischemic difficulties and in alleviating such associated conditions as causalgia makes it evident that sympathectomy might also be of benefit in attempting to correct certain circulatory conditions which sometimes follow the operative treatment of aneurysms and fistulas. Similarly experience with sympathectomy in other disorders in which blood flow through an important artery has been interrupted by disease, injury or operation suggests that this procedure would be of value in the problem under discussion. It is the purpose of this communication to record the results of this procedure in thirty-eight cases.*

Circulatory disorders after the operative cure of aneurysms and fistulas can be lessened by careful tests for collateral circulation as a guide to the selection of the proper time for operation, and by exact operative technique which insures avoidance of injury to the collateral blood supply. They can be eliminated for all practical purposes when the continuity of blood flow through the involved artery is maintained or restored by means of some reparative procedure methods which can be successfully applied to a considerable number of cases if this possibility is kept in mind and is utilized whenever applicable.² Nevertheless these difficulties do occur occasionally in spite of all efforts to avoid them.

CLINICAL MATERIAL

In the present series of cases, 290 aneurysms and fistulas were operated upon. 13 cases were observed in which a satisfactory "cure" by thrombosis occurred and an additional 63 cases were studied following operative cure performed elsewhere by other surgeons. Sympathectomy was performed before or at the time of operation upon 76 of the 290 patients whom I treated by operation and upon one of the 62 who had been operated upon by others, and

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Presented to the A.S.S.A. —

of a popliteal aneurysm and noted progressive thrombosis of the sac within a few days. An apparently satisfactory cure was obtained which obviated the necessity for operative treatment. In the present series of cases extension of the mural thrombus within the sac was often noted and in two instances a "cure" by thrombosis followed sympathectomy. Since spontaneous cure by thrombosis occurs occasionally it is impossible to state that a cause-effect relationship exists when a "cure" follows sympathectomy although the march of events in certain cases would suggest this to be true.

SUMMARY

1. A series of seventy-eight cases is reviewed in which sympathectomy was used as an adjunct in the operative treatment of aneurysms and arteriovenous fistulas.

2. The indications for this procedure are outlined.

3. Its value and its limitations are discussed.

4. Sympathectomy is a valuable aid in the treatment of aneurysms and fistulas. It does not however afford a guarantee against ischemic difficulties.

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The chief indications for operation have been as follows (1) distressing sensitivity of the limb to cold, (2) associated severe peripheral nerve damage in limbs in which the circulation was definitely impaired, (3) persistent edema, (4) ischemic nerve paralysis, (5) causalgia relieved temporarily but not cured by sympathetic blocks, (6) obviously impending gangrene, (7) evidence of sympathetic overactivity, with or without poor collateral circulation in a limb in which another arteriovenous fistula required excision

In three of the cases included (Cases 6, 7, and 8, Table V), sympathetic interruption was carried out by surgeons in other hospital installations. In one of them (Case 7 Table V) alcohol injection was performed. In the remainder, sympathectomy was carried out. Ganglionectomy through an anterior extraperitoneal approach was performed for the lower extremities, the Smithwick type of preganglionic operation was done for the upper extremities. Sympathetic interruption was carried out in twenty one lower and in eighteen upper extremities. No deaths and no serious complications occurred.

RESULTS OF THE PROCEDURE

The data concerning the thirty eight cases are summarized in Tables II to V, being grouped in the various tables according to the primary indication for sympathectomy. In many cases there were several circumstances which influenced the decision to perform sympathectomy. These and other relevant data are included in the tables.

SYMPATHECTOMY PERFORMED BECAUSE OF SENSITIVITY OF THE LIMB TO COLD

The commonest circulatory difficulty for which sympathetic interruption was carried out was sensitivity of the affected limb to cold. The data upon 17 such cases are summarized in Table II. Nine patients had arterial aneurysms and 8 had arteriovenous fistulas. Nine patients had involvement of an upper extremity and 8 had involvement of a lower extremity. The vascular lesions for which arterial ligation had been necessary involved the subclavian artery in 3 cases, the axillary in 1, the brachial in 5, the external iliac in 1, the femoral in 6 and the popliteal in 1. In one instance the aneurysm had been "cured" by spontaneous thrombosis; in the other cases excision of the lesion had been carried out. Seven of these operations had been performed overseas and 9 at the Mayo General Hospital. The duration of the lesion at the time of operation ranged from 1 to 4 months (average 1.6 months) in the first group, and from 2.5 to 11 months (average 5.7 months) in the second.

All the patients had annoying coldness of the affected hand or foot upon exposure to cold and most of them had cyanosis mild in some, severe in others. All had discomfort during such exposure, by some this was described as an aching, by others as a burning or tingling sensation. Most of them had some degree of numbness of fingers or toes and nearly all complained of stiffness of fingers or toes. When paresis was present it was aggravated during exposure to cold, and existing pain, paresthesias, or hypesthesia usually became more

it was carried out in 2 of the 13 cases in which a "cure" by thrombosis subsequently occurred (Table I). Sympathectomy was performed after operation in 19, or 8.9 per cent, of the first group of cases and in 18, or 29 per cent, of the second. Sympathectomy was also performed subsequently in one patient who had undergone a "spontaneous cure."

TABLE I SYMPATHECTOMY IN CASES OF ANEURYSM AND ARTERIOVENOUS FISTULA

	PATIENTS OPERATED UPON AT MAYO GENERAL HOSPITAL			PATIENTS OPERATED UPON ELSEWHERE			PATIENTS IN WHOM "CURE" BY THROMBOSIS OCCURRED		
	A V FISTULA	ANEURYSM	ALL	A V FISTULA	ANEURYSM	ALL	A V FISTULA	ANEURYSM	ALL
Patients sympathectomized before or at time of operation or with "spontaneous cure"									
No	47	29	76	0	1	1	1	1	2
Per cent of total	22.9	34.5	26.2	0	3.4	1.6	2.9	12.5	13.4
Patients without sympathectomy before operation or "spontaneous cure"									
Patients sympathectomized after operation or "spontaneous cure"	159	55	214	34	24	62	4	7	11
No	11	8	19	9	10	19	0	1	1
Per cent of those not previously sympathectomized	6.9	14.5	8.9	23.5	33.7	29	0	14.3	9.1
Total patients sympathectomized									
No	58	37	95	8	11	19	1	2	3
Per cent of all cases	27.7	44	32.9	21.5	39.3	30.6	2.9	25	23.1
Total No. Cases	206	84	290	34	24	62	5	8	13

It is of interest that sympathectomy was carried out before or at the time of operation in 26.2 per cent of the group operated upon at the Mayo General Hospital and in only 1.6 per cent of the group operated upon elsewhere and that the incidence of sympathectomy before and after operation was essentially the same in the two groups (32.8 and 30.6 respectively). It is also interesting that sympathectomy was performed more frequently in cases of arterial aneurysm than in cases of arteriovenous fistula the percentage of cases of arterial aneurysm in which this procedure was carried out after operation being 14.8 in the group treated at the Mayo General Hospital and 33.7 in the group treated elsewhere whereas the percentage of cases of arteriovenous fistulas in which the procedure was carried out was 6.9 and 23.5 in the two groups. Similarly the percentage in which sympathectomy was performed either before or after operation was 44 in cases of arterial aneurysm and 27.7 in cases of arteriovenous fistula in the first group, and 39.3 in cases of aneurysm and 23.5 in cases of fistula in the second group.

intense. The affected hand or foot was generally warm and well colored in a warm environment. One patient (Case 5) for example had a warm well colored foot at all times under ordinary circumstances and showed no evidence of circulatory insufficiency except for the usual fatigue on exercise. He lived however in Minnesota and on exposure to cold the foot became icy cold and numb and ached severely. There was no improvement in this regard over a period of months. Complete relief followed sympathetic ganglionectomy. It was my practice to test each patient's ability to withstand exposure to cold. If only mild manifestations of sensitivity were present or if more marked symptoms occurred on exposure to severe cold in a patient who planned to live in a warm part of the country it was felt that the condition would cause little discomfort or disability. It was equally apparent that such symptoms were of considerable importance to persons who lived in a cold climate. The situation was explained to these patients; they were allowed to compare the reaction of the limb to a cold environment under ordinary circumstances and during a period of sympathetic procaine anesthesia and the choice of operation was offered to them. Except for a very few who felt that their work, vocations and general interests made prolonged exposure to the outside cold unnecessary all elected to have sympathectomy performed. The advice of their few patients who had undergone this procedure for similar complaints undoubtedly influenced the choice of many.

It will be noted that eight of the patients had in addition associated peripheral nerve lesions. A few had evidence of sympathetic overactivity under ordinary environmental circumstances and in one this vasospasm was rather pronounced. Several had obvious evidence of unpaired circulation. One patient had mild causalgia. One had sustained a fairly severe frostbite of the feet at the time of the injury which produced the external iliac aneurysm. In this patient the frostbite contributed to the cold sensitivity which was however much more severe in the limb in which the external iliac artery had been divided.

The results of sympathectomy were excellent. In all except two patients complete relief was obtained and in these two definite improvement was noted. The pain was much improved in the patient with causalgia as it was in all other instances in which pain had been present with the exception of the patient with frostbite who continued to have some mild burning in the foot. The nerve regeneration was as satisfactory as could be expected from the trauma sustained.

SYMPATHECTOMY PERFORMED BECAUSE OF ASSOCIATED PARALYSIS AND IMPAIRED CIRCULATION

In Table III data are given concerning five patients upon whom sympathectomy was performed in an attempt to improve unpaired circulation in order to afford maximal opportunity for repair of extensively damaged peripheral nerves. In all there was evidence of reduced blood flow and severe nerve damage. Most of them were cases in which sympathectomy had been consid-

TABLE II SYMPATHETOMY PERFORMED AFTER OPERATION FOR ANEURYSM OR FISTULA, OR AFTER "SPONTANEOUS CLIP," INDICATION—COLD SENSITIVITY

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND OPERATION (IN MO)	INTERVAL BETWEEN OPERATION AND SYMPATHETOMY (IN MO)	TYPE OF OPERATION	COMMENT	RESULT
<i>Intercostal Fistulas</i>						
1	Subclavian	4	5	E*	Extreme <i>cs</i> , fatigue	Relief
2	Subclavian	4	2	E	Marked <i>cs</i> , fatigue	Relief
3	Subclavian	3	2	E		Relief
4	Brachial	2	2	E	Marked <i>cs</i> vaso spasm, pain aggravated by cold exposure, ulnar palsy, fistula discovered during neurovascular exploration	loss of pain
5	Femoral	25	3	E	Marked <i>cs</i>	Relief
6	Femoral	22	4	E*		Relief
7	Femoral	1	35	E*		Relief
8	Femoral	1	5	E*	Partial sciatic paralysis, pain in foot	Relief, pain improved
<i>Internal Aneurysms</i>						
9	Axillary	5	15	E	Also severe plexus injury circulation impaired	Relief, circulation improved, nerve return satisfactory except for residual lesion transplant
10	Brachial	6	07	E	Also mild calcification an palsy circulation impaired	Relief, circulation improved, calcification largely relieved nerve return satisfactory
11	Brachial	77	0"	E	Cold sensitivity before and after operation ulnar palsy	Relief nerve return satisfactory
12	Brachial	7	1	E	Also median palsy	Much improved, satisfactory nerve return
13	Brachial	"spontaneous cure 15 excision thrombosed artery 6	6	E Freckles thrombosed artery	Also median palsy neurolysis	Relief excellent return of nerve function
14	Ext iliac	11	1	E	Also frostbite marked <i>cs</i> with pain and hypesthesia	<i>CS</i> persists though considerably improved burning persists
15	Femoral	1	6	E*	Marked <i>cs</i>	Relief
16	Femoral	1	5	E*		Relief
17	Popliteal	12	65	E*	Sciatic palsy pain in foot	Relief pain improved

*In this and following tables an asterisk signifies that the operation was performed overseas. Abbreviations in this and following tables: E excision A aneurysmorrhaphy or similar procedure A E aneurysmorrhaphy or similar procedure followed by excision of associated cold sensitivity

TABLE IV SYMPATHECTOMY PERFORMED AFTER OPERATION FOR ANEURYSM OR ARTERIOVENOUS FISTULA, INDICATION—EDEMA

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND OPERATION (IN MO)	INTERVAL BETWEEN OPERATION AND SYMPATHECTOMY (IN MO)	TYPE OF OPERATION	COMMENT	RESULT
<i>Arteriovenous Fistulas</i>						
1	Popliteal	3	0.5	E	Saccular aneurysm as well as A V, subcutaneous rupture had caused peroneal palsy, after operation had fairly marked edema, foot was cool	Marked improvement, foot warmer, edema much less subsequently disappeared, good nerve return
2	Popliteal	6	1	E	Marked edema, foot cool	Edema moderately improved, foot warm
3	Posterior tibial	2	0.8	E	"	"
4	Posterior tibial	2	6	E*	edema from sympathectomy blocks but no lasting effect Persistent edema, some cyanosis of foot	Edema considerably less
<i>Arterial Aneurysms</i>						
5	Popliteal	0.5	2.5	A*	Marked edema, cyanosis of foot, ulcers of leg peroneal palsy tibial palsy questionably due to postoperative ischemia	Marked improvement, edema minimal, ulcers healed

gradually increasing periods of exercise. Sympathetic blocks had resulted either in only transient diminution in swelling or in no noticeable effect except for temporary warmth and dryness of the foot. In addition to edema two patients had paralysis of nerves; all had some cyanosis, coolness of the affected foot, or hyperhidrosis and one had indolent ulcers. Four had an arteriovenous fistula, 1 an arterial aneurysm, three a popliteal fistula or aneurysm, and two a posterior tibial fistula. Two patients had been operated upon overseas at a time when the vascular lesion was of two weeks' duration and two months' duration, respectively. Three patients were operated upon at the Mayo General Hospital, the lesions were of two, three, and six months' duration. Sympathectomy was performed from two weeks to six months after operation. The results were fair in one case (Case 2), somewhat better in another (Case 4), and excellent in the others. In addition to the effect upon the edema, warmth and good color prevailed in all the limbs treated. Satisfactory return of nerve function took place.

TABLE III SYMPATHECTOMY PERFORMED AFTER OPERATION FOR ANEURYSM OR ARTERIOVENOUS FISTULA, INDICATION—REDUCED BLOOD SUPPLY AND SEVERE NERVE DAMAGE

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND OPERATION (IN MO)	INTERVAL BETWEEN OPERATION AND SYMPATHECTOMY (IN MO)	TYPE OF OPERATION	COMMENT	RESULT
<i>Arteriovenous Fistulas</i>						
1	Axillary	65	07	E	Had had lysis of brachial plexus and ulnar neurorraphy	Circulation excellent, good nerve return
2	Axillary	5	1	E	Had had lysis of plexus and suture of posterior cord, also some c.s.	Circulation better, slight c.s. remains nerve return satisfactory
<i>Arterial Aneurysms</i>						
3	Subclavian	25	07	A	Severe plexus damage, no surgical repair possible, causalgia, improved after operation	Circulation much improved, good nerve return except for posterior cord, comfortable
4	Axillary	25	1	A	Extensive plexus damage, circulation impaired, much sensitivity of hand	Hypersensitivity of hand relieved, some immediate nerve return subsequent satisfactory progress
5	Brachial	1	15	E*	Had lysis of ulnar and suture median nerve, some c.s.	C.S. relieved, satisfactory nerve return, circulation improved

ered before operation but had been deferred because of evidence of excellent collateral circulation and in the hope that the damage to the nerve might prove at exploration to be due in large part to pressure of the aneurysm or might prove to be less severe than was anticipated. In all of them the neurological condition observed at operation was disappointing in this regard. In addition, one patient had extremely impaired circulation, one patient had extreme hyperesthesia of the hand and two had some sensitivity of the part to cold. It will be noted that four were cases of arterial aneurysm and two were cases of arteriovenous fistula. It will also be noted that all except one were cases of injury to the brachial plexus and that all the vascular lesions involved the subclavian, axillary, or brachial vessels. The results were gratifying. Signs of nerve regeneration indicate as satisfactory progress as might be hoped for considering the extent of the nerve damage. The circulation in the limb was visibly improved. The sensitivity to cold was relieved or improved.

SYMPATHECTOMY PERFORMED BECAUSE OF PERSISTENT EDEMA

Data concerning six patients in whom sympathectomy was performed because of persistent edema are given in Table IV. The edema in these patients ranged from moderate to massive. All had failed to improve under conservative measures such as rest and elevation of the limb, elastic support and

TABLE V—CONT'D

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND OPERATION (IN MO)	INTERVAL BETWEEN OPERATION AND SYMPATHETOMY (IN MO)	TYPE OF OPERATION	COMMENT	RESULT
<i>Arterial Aneurysm—Cont'd</i>						
7	Axillary	27	Same day	E*	Obviously impending gangrene of hand especially of thumb with marked ischemic paralysis followed operation also had traumatic plexus injury treated by alcohol injection	Gangrene limited to thumb which was amputated slow steady but incomplete recovery from ischemic and traumatic paralysis
8	Femoral	30	One day	A*	Foot extremely cold and pale after operation	Excellent good color and warmth
9	Brachial	1	10	E*	Causalgia severe and severe plexus injury including irreparable damage to musculocutaneous nerve	Causalgia relieved cold sensitivity improved nerve return satisfactory
10	Popliteal	05	070	E*	Causalgia and peroneal paralysis followed operation	Causalgia much improved
11	Profound femoral	2	02	E	Moderate causalgia temporarily relieved by sympathetic block tibial palsy definite hypochondriasis	Immediate relief slight subsequent complete relief with exercise and encouragement

SYMPATHETOMY PERFORMED BECAUSE OF ISCHEMIC LESIONS CAUSALGIA AND OTHER CONDITIONS

In Table V data are summarized concerning 11 patients upon whom sympathectomy was performed for various other indications. Six were cases of arterial aneurysms and 5 cases of arteriovenous fistula. The operations upon these lesions were performed overseas in 7 and at the Mayo General Hospital in 4 cases.

Ischemic paralysis was the primary indication for sympathectomy in 3 patients (Cases 1, 2 and 6). In 2 the neurological difficulty followed operation for the cure of a femoral arteriovenous fistula. The clinical records of these patients contained no data concerning the state of collateral circulation before operation. In one patient there was extensor paralysis of two toes anesthesia of the foot and stocking hypesthesia almost up to the knee. Improvement began promptly after sympathectomy and progressed over the ensuing weeks. Motor power returned to the toes the hypesthesia disappeared from the leg and the foot was no longer anesthetic though still hypesthetic. The other patient had a stocking anesthesia with complete sciatic paralysis after operation. Return of function in the tibial nerve was prompt but at the time of a lumbosacral myelogram the patient had complete peroneal motor loss and nearly complete

TABLE V SYMPATHECTOMY PERFORMED AFTER OPERATION FOR ANEURYSM OR ARTERIOVENOUS FISTULA, MISCELLANEOUS INDICATION

CASE NO	LOCATION OF LESION	INTERVAL BETWEEN INJURY AND OPERATION (IN MO)	INTERVAL BETWEEN OPERATION AND SYMPATHECTOMY (IN MO)	TYPE OF OPERATION	COMMENT	RESULT
<i>Arteriovenous Fistulas</i>						
1	Femoral	2	3	Transcavalicular ligation*	Storking hyposthesia up to just below knee foot largely anesthetic, extensor paralysis toes 1 and 2 ischemic pulse following operation	Anesthesia gone hyposthesia only of foot regained extension of toes improvement began within few days after sympathectomy
2	Femoral	0*	3	E*	Foot anesthesia and complete tibial and peroneal paralysis followed operation regained tibial function promptly, on admission peroneal motor loss complete, sensory almost complete	Improvement began within few days complete recovery
3	External iliac	17	33	E*	Some c.s. poor collateral circulation a second (hypogastric) A.V. fistula remained to be excised	Excellent good circulation following excision of hypogastric fistula no c.s.
4	Circumference of foot	7	3	E	Hyperthrombotic and cyanosis followed excision post tibial A.V., peroneal and anterior tibial A.V. fistulas remained to be excised	Foot remained warm dry and well colored after remaining fistulas were excised
5	Femoral	85	0*	E	Foot had excellent circulation until 6th PO day when arterial and venous thrombosis occurred with coldness numbness and paresis of foot	Some improvement with descent of cold level gangrene of toes and sole of foot occurred however
<i>Arterial Aneurysms</i>						
6	Brachial	15	3	E*	Complete paralysis upper extremity after injury after several months gauntlet type anesthesia etc suggested residual paralysis was largely ischemic hand cold cyanotic	Marked improvement began after sympathectomy steady significant but incomplete return of function

tomy was performed the day after aneurysmorrhaphy because the foot was alarmingly cold and pale. The foot regained good warmth and color.

In three patients sympathectomy was done because of causalgia (Cases 9, 10 and 11). All had peripheral nerve damage and one had severe sensitivity to cold. In all temporary relief but no lasting effect followed a series of sympathetic blocks. The causalgia was relieved in one and much improved in another. The third patient continued to complain of pain after operation. He had in addition other complaints which gave evidence of hypochondriasis. The pain disappeared with reassurance and exercise.

There remains to be discussed the effect of sympathectomy upon the fatigue on exercise which occurs in a striking fashion in the lower extremity after ligation of the iliac, femoral or popliteal artery and in a less noticeable degree in the upper extremity after ligation of the subclavian axillary or brachial artery. Ability to exercise the upper extremity was measured manometrically by having the patient squeeze once every second a rubber bulb which was connected through a 5 gallon bottle with a mercury manometer. The number of such squeezing movements performed before prohibited by fatigue were recorded as well as the height of the manometer at the end of the test. Exercise tolerance in the lower extremities was estimated by the number of yards a patient could walk at a normal pace before he had to stop because of fatigue or less commonly cramps in the calf. The distance was measured by a pedometer or by having the patient walk over a measured course. Unfortunately the number of patients upon whom such studies were carried out before and after sympathectomy and in whom there was no real limitation to exercise because of associated fractures or motor paralysis is too few to make statistically significant analysis possible. Those patients who had sympathectomy after ligation of the femoral or popliteal artery for the cure of aneurysm or fistula had fatigue or cramps after walking an average of 0.82 mile which is approximately the same as in those patients treated for similar lesions without sympathectomy.¹ Many of the patients showed no improvement in tests for exercise tolerance after sympathectomy; many showed only slight improvement. A few, however, noted a striking increase in exercise tolerance. For example on admission five and one half months after excision of a femoral aneurysm one patient (Case 15 Table II) was forced to stop after walking one half mile because of aching and fatigue in the calf. Sympathectomy was performed because of sensitivity of the foot to cold. Within two weeks he could walk two miles before getting fatigue in the calf. Such improvement is exceptional, however.

Comparison of the series of patients operated upon overusers and those treated at the Mayo General Hospital may be profitable from the standpoint of factors influencing the occurrence of postoperative difficulties for which sympathectomy is required. If only those cases are considered in which the main arteries to the extremities were involved (innominate, subclavian, axillary, brachial, external iliac, common femoral and popliteal arteries) 17 of 43 patients in the first group were treated by sympathectomy (39.5 per cent) and 17 of 184 patients in the second group (9.2 per cent). If those cases are

sensory loss. The neurological condition appeared stationary. Return of peroneal function was noted within a few days after sympathectomy and progressed steadily thereafter to complete recovery. The third patient had paralysis of the upper extremity after injury, when he was examined 3 months after excision of an axillary aneurysm and 4½ months after injury the gauntlet type of anesthesia and other findings made it evident that the residual paralysis was largely ischemic in nature. The hand was cold and cyanotic and ached upon exposure to cold. Improvement was noted shortly after sympathectomy the anesthesia receding in a glove-like fashion. Nine months after sympathectomy there was normal sensation except for hypesthesia of the dorsum of the hand and anesthesia of the palmar surface of the fingers. Return of motor function had been considerable but incomplete. The hand was well colored, warmer and withstood exposure to cold fairly well.

Sympathectomy was carried out in two patients (Cases 3 and 4) with multiple arteriovenous fistulas. In the one there was some sensitivity to cold and evidence of very poor collateral circulation following excision overseas of an external iliac fistula. Another fistula which proved at operation to involve the neighboring hypogastric vessels remained to be excised. Immediately after sympathectomy the collateral circulation was retested and found adequate and the hypogastric fistula was excised. The limb maintained excellent circulation. The other patient had a congenital cirroid aneurysm of the foot with distinct fistulas of the anterior and posterior tibial and peroneal vessels. Excision of the posterior tibial fistula was followed by extreme hyperdrosis and cyanosis of the foot which persisted over a period of months. The foot remained warm and dry after sympathectomy. The other fistulas were resected without difficulty.

Sympathetic interruption was carried out in two patients because of obvious impending gangrene (Cases 5 and 7). One patient who had mam-

terial and venous thrombosis had occurred. There was little improvement in circulation during spinal anesthesia but because of the desperate situation sympathectomy was performed. Actually the cold level decreased and sensation improved. The improvement in circulation was insufficient however to prevent gangrene of the toes and sole of the foot and amputation was necessary. The other patient was operated upon overseas nearly three months after an injury which had produced partial paralysis of the brachial plexus. An aneurysm of the axillary artery which was unexpectedly encountered was excised. After operation the hand was cold and cyanotic and the thumb in particular seemed devoid of circulation. Successful alcohol injection of the dorsal sympathetics was accomplished. Gangrene of the thumb occurred and the thumb was amputated. In the rest of the hand there was restoration of fairly good circulation. A definite ischemic paralysis had been added to the pre-existing damage to the plexus. Steady improvement in nerve function followed but recovery was incomplete. In a third patient (Case 8) sympathect

tomy was performed the day after aneurysmorrhaphy because the foot was alarmingly cold and pale. The foot regained good warmth and color.

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eliminated in which sympathectomy had been carried out before or at the time of operation and also those cases in which the continuity of blood flow through the affected artery was successfully maintained. The figures for the first group are 17 of 42 cases, or 40.5 per cent, and for the second group 17 of 108 cases, or 15.7 per cent. In each group sympathectomy was performed in one case partly because of the presence of another arteriovenous fistula which required excision. In general, the duration of the vascular lesion was shorter in the first group than in the second. The duration ranged from a few days to 43 months in the first group or an average of 1.6 months. In only about 17 per cent was the duration 3 months or longer. In the second group the duration ranged from 6 weeks to 15 months or an average of 5.1 months, excluding one case of 13 years' duration. In about 85 per cent the duration was 3 months or more.

Unfortunately the two groups are not entirely comparable. Early operation was apparently forced by complicating circumstances in a somewhat higher percentage of the patients operated on overseas than in those treated at the Mayo General Hospital. The patients in the first group were operated upon by numerous surgeons, whereas those in the second were treated by a few surgeons whose work was confined to the care of vascular disorders. Careful testing of the collateral circulation before operation was a routine procedure in the latter cases; judging from the clinical case records and interrogation of the patients, such tests were not carried out in those operated upon overseas. It is obvious then that the two groups are not comparable regarding these important factors. Nevertheless the need for sympathectomy in a much higher percentage of these patients operated upon overseas suggests that postoperative circulatory difficulties are less frequent when operation is performed upon aneurysms or fistulas of relatively long duration. This hypothesis can probably be expressed more accurately by saying that the incidence of such difficulties will be less when the collateral circulation is established as adequate before surgery is undertaken, for although the collateral circulation tends to be better in cases of long duration, especially in the case of arteriovenous fistulas, there are frequent exceptions in which good collateral circulation is present in lesions of short duration and poor collateral circulation in lesions of long duration.

DISCUSSION

Circulatory difficulties following operative cure of peripheral aneurysms

cases in which it is possible to maintain the continuity of blood flow through the affected artery. In spite of extreme care, however, certain patients treated for aneurysm or fistula are likely to have some circulatory disorders. These will not always be apparent from casual observation of the patient upon the wards. If it is our desire to provide these patients with the best possible limbs

and not merely to avoid such gross ischemic disasters as gangrene more careful inquiry into the circulatory status is necessary. It is important to test the exercise tolerance of these limbs to make certain that no distressing symptoms upon exposure to cold, no persistent edema and no painful states or ischemic paralysis are present and to be certain that the return of nerve function in cases of peripheral nerve injury is not compromised by inadequate circulation. In certain of these sequelae sympathectomy is of considerable benefit.

Next to diminished ability to exercise the limb without fatigue, cold sensitivity of the part is the commonest circulatory difficulty. In mild degree or in patients who live in warm climates this is apt to cause no real discomfort or disability. When it exists in rather severe degree in patients whose place of residence and type of work require exposure to cold temperatures the symptoms are distressing and often disabling. Sympathectomy yields excellent results in such cases. Preliminary sympathetic procaine blocks followed by exposure to a cold environment serve as a good guide to what may be expected of operative sympathectomy.

Persistent edema of significant degree is an unusual symptom. If present it should be treated by rest and elevation of the limb, elastic support and graduated activity with the limb dependent. If such measures are ineffectual sympathetic blocks or sympathectomy may be of real value. Unfortunately sympathetic blocks are not a completely reliable index to what may result from permanent sympathetic interruption. If these blocks cause transient but not permanent diminution in swelling sympathectomy is likely to be very helpful. If on the other hand no effect upon the edema is noted from procaine blocks sympathectomy may also in certain cases be of benefit.

When ischemic difficulties are present the efficacy of sympathectomy in correcting them depends upon the capacity of the collateral circulation to improve through the elimination of persistent or intermittent vasoconstriction and the maintenance of a state of vasodilatation. As with other disorders in which arterial blood flow has been interrupted this capacity varies in different individuals. In my experience sympathectomy has been strikingly successful in instances of ischemic nerve paralysis. The results in the two cases reported in which gangrene was imminent were less successful. In such cases the procedure should be given consideration however even if the limb shows only slight improvement with sympathetic block or spinal anesthesia. Occasionally in instances of impending or spreading gangrene due to occlusion of arteries from other causes sympathectomy has produced striking benefit even after such poor response to preliminary tests.

It is my belief that sympathectomy is indicated in cases in which severe nerve damage is associated with obviously impaired circulation and that the evidence of good nerve return in these cases has justified the procedure. Unfortunately there are available no carefully controlled clinical studies comparing nerve regeneration in such cases in which sympathetic interruption has and has not been carried out. Sympathetic procaine block does not invariably give reliable information regarding the results which may follow

sympathectomy. If the nerve paralysis has not brought about sensory loss in the entire hand or foot, any improvement in circulation from sympathetic procaine block is readily demonstrable by skin temperature changes in the normally innervated digits. If, however, there is normal sensation (and intact sympathetic innervation) to no part of the hand or foot no rise in skin temperature is ordinarily noted during sympathetic procaine anesthesia. That sympathectomy may actually increase the circulation in such cases is suggested by the decreased tendency to dependent cyanosis which is sometimes noted after operation by diminution in cold sensitivity occasionally by increase in oscillography, but particularly by the striking improvement in nerve function which so often follows when part of the neurological damage is ischemic in nature. Obviously, when there is anesthesia of portions of the skin and consequently local sympathetic denervation sympathectomy will not alter the tonus of blood vessels in the anesthetic skin. It is equally apparent that the blood flow in the limb can be increased by elimination of vasoconstriction from the vessels of the limb as a whole.

SUMMARY

- 1 The results of sympathectomy in attempting to correct certain circulatory difficulties following the operative cure of aneurysm or arteriovenous fistula have been studied in thirty eight cases.
- 2 The indications for this procedure are outlined.
- 3 Sympathectomy seems to offer real aid in the correction of these post operative circulatory disorders although there are limitations to its achievements.

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REPAIR OF SKULL DEFECTS

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THE management of cranial defects has been repeatedly stressed in the literature in recent years, with particular emphasis on tantalum during the war. Many types of material have been used successfully and it is not necessary to repeat the various indications, contraindications, methods of preparation, and operative techniques at this time. Rather, the emphasis is on experiences using tantalum, bone, and cartilage in various situations during the past 3½ years on the neurosurgical and plastic surgical services at Valley Forge General Hospital. Sufficient time has elapsed to allow evaluation of some of the patients operated upon earlier both here and elsewhere, and certain problems have been encountered with each substance employed which deserves consideration for the proper management of cases of this type. One of us (W. G. P.) in collaboration with Robertson⁴ has recorded results with the use of tantalum alone in 254 instances. This series now totals 279.

Tantalum has been the material preferred by the majority of the military neurosurgeons because of its malleability, strength and limited tissue reaction. Its use has been justified further by the pressure of a great number of casualties during active warfare which demanded a simple, uniform method of cranioplasty easily and rapidly performed by many surgeons, preferably in one stage. It has been possible to insert a tantalum plate successfully in a soiled field² or as early as 3 to 4 weeks after an active infection. However, the best end results have been obtained by waiting at least six months prior to further attempts at cranioplasty in cases of this type. This fact was recently stressed by Bradford and Livingston,¹ and is even more important when the use of bone is contemplated as it is much less tolerated in latently infected wounds. In either event, the patient is always well prepared with penicillin and sulfadiazine pre and postoperatively. On the whole, the use of the tantalum has proved very satisfactory, particularly in large defects over the vertex. However, attention must be directed toward adequate scalp nutrition as previously pointed out² in that complete exposure of the bony margins is necessary for fixation of the plate.

Many have advocated multiple perforations of the tantalum plate prior to its insertion to facilitate adequate subsequent absorption, to allow greater dissemination of local penicillin in event of infection, to provide an increased bed for adhesions and better fixation, and to improve vascularity in questionably viable superficial scars. Borderline cases of the latter type should be revised according to the principles already outlined² prior to or during cranioplasty. Since it is not possible to insert a plate "watertight" and inasmuch as the ultimate scar superficial and deep to the tantalum is ample for

A



B

FIG 1 A and B—A Postoperative tantalum cranioplasty over both supraorbital ridges. One small depression above right eyebrow at site of perforation in plate. B Same patient ten months later with two depressions above right supraorbital ridge in vicinity of two large perforations in plate. Beginning depression above left eyebrow medially.

stabilization, it is not felt that such orifices present any material advantage. Further, the scar extending through such openings may contract over a period of time and produce noticeable disfigurement of the scalp, particularly in the frontal regions (see Fig 1)

The possible disadvantages in the use of tantalum may be the deleterious results of subsequent deep x ray therapy or diathermy, and its radioactivity in event later complications develop necessitating roentgenographic examination, long term effects on the adjacent tissues are not yet available. Tantalum should be avoided where only limited exposure of the bony margins is possible, in children, in whom the growth factor must be considered and further bone regeneration anticipated, and in restoration of the complicated bony contours in vicinity of the supraorbital ridges, glabella, and nasal and zygomatic processes of the frontal bone. In these instances, the use of autogenous bone, either rib or ilium, is preferred. Both are well adapted to attain as nearly as possible the normal outlines of the skull.



C

Fig 1 C—Roentgenogram showing site of perforations in tantalum plate corresponding to previous scalp depressions.

At least eight cases have been observed recently in which a tantalum plate had been inserted over the supraorbital ridge elsewhere without achieving satisfactory cosmetic restoration. In these patients, the plate was found to be either too high (see Fig 2) or too low (see Fig 3), with such deformity as to have the individual seek further repair. Several procedures had been performed, usually in an attempt to achieve an improved result prior to transfer here for "insertion of cartilage or bone." It is preferable not to use either of these substances in the presence of tantalum because firm union does



A



B

FIG 2—A Tantalum cranioplasty with incomplete restoration of right supraorbital ridge. B Roentgenogram showing tantalum plate deficient over right supraorbital ridge. Film reversed during processing.



A



B

FIG 3—A Tantalum plate too low laterally over left supraorbital ridge. B Roentgenogram demonstrating lateral distortion of left orbit due to low tantalum plate.



Fig 4—Postoperative x ray view in which the preorbital ridge was repaired initially with bone and completed later with tantalum



Fig 5—A Pulsating defect of right squamous portion of frontal bone. B Postoperative right squamous frontal cranioplasty completed with bone through old craniotomy scar



A



B

Fig 2—A Tantalum cranioplasty with incomplete restoration of right supraorbital ridge. B Roentgenogram showing tantalum plate deficient over right supraorbital ridge. Film reversed during processing.



A



B

Fig 3—A Tantalum plate too low laterally over left supraorbital ridge. B Roentgenogram demonstrating lateral distortion of left orbit due to low tantalum plate.

No form of fixation has proved advantageous as long as a good, firm head dressing is applied and kept in place for twelve to fourteen days. No drains have been employed, the wound being inspected and sutures removed in 3 to 5 days. There is less fluid accumulation beneath the scalp than after the use of tantalum. In the event of postoperative infection, sequestration with loss of part of the graft may take place, but it is unusual to lose the entire transplant under these circumstances.



FIG 7

Fig 7—Postoperative photograph of cranioplasty involving left squamous portion of frontal bone completed with bone which was inserted through marginal incisions to preserve previous remote pedicle flap.



FIG 8

Fig 8—Left orbitofrontal wound with associated defect. Completed remote flap in place. Coronal incision with reflection of flap for tantalum cranioplasty ten months later.

SUMMARY

The purpose of this report has been to call attention to three common methods of cranioplasty, namely, tantalum, bone, and cartilage. Each case must be evaluated as to the most suitable form of repair. The various situations in which these materials have been used most satisfactorily are now briefly reviewed.

Use of Bone

- 1 Small, pulsating defects particularly over the frontal regions including the glabella, supraorbital ridge, frontal sinus, zygomatic and nasal processes of the frontal bone

not result. Conversely, tantalum may be employed secondarily in large defects when bone was used for the initial repair of the supraorbital ridge (see Fig 4). The tantalum plate was, therefore, removed in each instance noted previously and cranioplasty completed with bone in five instances and revised with tantalum in the remaining three.



Fig 8—A Nonpulsating defect of left squamous portion of frontal bone. B Postoperative left squamous frontal cranioplasty completed with cartilage through previous craniotomy scar.

It is emphasized that it is not always possible or necessary to obtain complete operative exposure² especially if cortical exploration is not contemplated. Such instances include small defects over the frontal regions and the presence of a remote flap or split thickness graft. In these cases bone or cartilage has been inserted through the old craniotomy scar (see Figs 5 and 6), through marginal incisions of a previous flap (see Fig 7), or by reflecting varying portions of the flap if a considerable time interval has elapsed (see Fig 8). Bone has been used in pulsating defects and preserved cartilage in areas where pulsation is not manifested. The tendency of fresh cartilage to curl can be overcome by introducing multiple chips rather than a solid section. The cortical margins of the bone along the defect are rongueured away to expose the vascular surface. When bone is used, it may be taken from the ribs or ilium. The former can be split for additional grafting material.

REPAIR OF SCALP DEFECTS

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THE association of extensive craniocerebral and maxillofacial wounds incurred during modern warfare necessitates the close cooperation of both the neurologic and plastic surgeons not only during the acute reactive phase on the battlefield but also in the period of reconstruction following evacuation to the zone of the interior. Injuries of this type are often accompanied by considerable loss of skin, soft tissue, and bone. The type of incision at debridement is dictated often by the location and severity of the wound or the presence of complications. The procedure should take into consideration the need of later local direct or delayed flaps, grafts, cranioplasty, and cortical exploration. The methods employed successfully for scalp revision and closure during the reconstructive period on the neurologic and plastic surgical services at Valley Forge General Hospital may be applied during preliminary treatment behind the front lines and to similar injuries observed during civil life.

Closure of the scalp following debridement for craniocerebral wounds sustained in overseas theaters was usually accomplished by one or more of the following methods:

1. Approximation of the skin edges
2. Skin grafting
3. Advancement of direct single or double pedicle flaps

The use of delayed or remote flaps has been reserved almost entirely for the reconstruction centers in the zone of the interior.

In the majority of patients received here, some form of primary or secondary suture had been performed with or without local rotation of flaps. Many resulted in the formation of thin scalp scars with densely adherent dura and cortex (see Fig. 1). In other cases the cranial defect had been covered with a free skin graft (see Fig. 2). In still others the wound was open with exposure of the dura or cortex and with varying degrees of infection. In those with the outer table of the bone alone exposed, an improved bed for grafting was obtained by multiple small perforations to the diploe in order to produce granulations. Patients with open wounds have been treated with hot wet compresses, penicillin (local and systemic), and sulfadiazine as indicated. The simplicity of the definitive treatment depends upon having as few additional scars in the adjacent scalp as possible. Thus primary repair with skin grafts or primary closure of the wound rather than complicated shifting of flaps has made possible better final repairs. Replacement

2 Small to moderate sized defects in any location where only limited exposure can be effected due to possible interference with circulation of a pedicle flap. If extensive cranioplasty can be performed in multiple stages with bone or started with bone and completed with tantalum corresponding to the amount of exposure possible. The reverse situation is not desirable (bone used in the presence of tantalum) as firm union does not result.

3 Cranial defects in children

4 In cases where the following may be anticipated: deep x ray therapy, repeated diathermy to the head and neck, pneumoencephalography in the more severe craniocerebral injuries with dural penetration and likelihood of post traumatic convulsions.

Use of Cartilage

1 Small nonpulsating defects over the orbital areas, frontal sinus (particularly when outer wall alone is involved), and nasal processes of the frontal bone. This is important as cartilage does not always unite firmly with bone. Therefore if previous pulsation was present it will probably continue.

2 Small defects (nonpulsating) and slight depressed fractures through the outer table of the bone (particularly over the squamous portions of the frontal bone), either in open or closed head injuries in which extensive debridement had not been performed previously and no further late indications exist other than from the cosmetic standpoint.

3 To fill in small residual depressions when bone has been used. It is to be pointed out that this is not done in the presence of tantalum as firm union does not result.

4 To restore bony prominences of the face such as over the zygoma and its frontosphenoidal and temporal processes and orbital portion.

Use of Tantalum

1 Any region over the vertex where complete exposure can be obtained other than in the situations first cited in which cartilage or bone are preferable.

2 Any situation in which bone is contraindicated and complete exposure is possible for fixation. General physical condition of the individual pre or coexisting disability.

3 Extremely large defects for obvious reasons. If long enough time has elapsed in the presence of a remote flap its reflection should be possible for insertion of such a plate.

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A



B



C

FIG. 4. Extensive left orbital wound closed with split thickness graft prior to elevation. B. Previously delayed rect chest flap elevated to involved area following removal of free graft. C. Completed pedicle flap prior to cranioplasty.



Fig 1—A. Avulsion wound of right frontoparietal region complicated by brain abscess with red's at thin atrophied scalp near. B. Previously delayed direct flap applied to scalp after removal of superficial near C. Completed flap covering scalp defect prior to cranioplasty.



A



B

Fig 4



Fig 4—A Left orbitofrontal wound with local frontal pedicle flap to lower lid defect. Frontal scalp repaired with split thickness graft. B Postoperative frontal cranial defect. C Nonpulsating midfrontal cranial defect repaired with cartilage through old craniotomy scar rather than coronal incision to preserve previously grafted frontal scalp.

Fig —Patient referred for postoperative infection following titanium cranioplasty. Wound debrided, plate removed and closure effected only after a left parietal relaxing incision was made.

of thin scalp scars or skin grafts in these cases is necessary for subsequent cranioplasty, dural repair, cortical lysis, or extirpation. The following methods have been used:

1. Excision of narrow craniotomy scars has been satisfactory usually for ordinary cranioplasty and/or cortical exploration. The amount of tension resulting during closure is an important factor for adequate wound healing. A certain amount of stretching of the adjacent tissues and undermining of the margins of the scalp defect is possible. This method, however, has its limitations, as shown in Fig. 3. The majority of patients received here had had repairs done by curvilinear incisions. The tripod incision or its isle of man



Fig. 3—Closure of right frontal incision over tantalum plate elsewhere with distortion of adjacent scalp and brow. Tantalum removed on two occasions due to necrosis and infection. Replacement of soft tissue loss with delayed arm flap.

modification, advised so commonly in World War I was used rarely due to poor wound healing at the apex of the flaps. A large craniotomy type of flap was employed occasionally. In these circumstances the wound of entry was included either in the lateral limb of the incision or in its midportion (when small). Previous S and Z shaped exposures including the point of entrance in the central limb were encountered also.

2. Coronal incisions are ideal for complete exposure of extensive defects in the frontal region. However, if the scalp scar is either very dense and

disfiguring or extremely thinned and adherent primary revision is preferable prior to cranioplasty. Local frontal pedicle flaps from areas with normal underlying bone may be used in the reconstruction of the eyelids and repaired with a split thickness graft in the presence of a small associated cranial defect. Such a lesion can be repaired easily by entering the previous craniotomy scar and inserting bone if the defect pulsates and by inserting cartilage if no pulsation is present (see Fig 4). In the larger defects where a coronal incision is planned other provisions for facial repairs must be made to maintain the integrity of the frontal scalp. A contemplated coronal flap should be delayed if there is any doubt about the blood supply in cases where the previous wounds or operations involved the supraorbital vessels.

3 In the temporal region there is usually sufficient vascularity to employ the usual craniotomy incision but attention must be directed toward a broad enough unscarred pedicle to insure adequate blood supply.



Fig 7. Tubed pedicle flap to right frontotemporoparietal area. Dural repair and application of flap accomplished at one procedure; cranioplasty being performed at a later date. Preliminary surgery was done previously at Cushing General Hospital.

4 Relaxing incisions are useful often in small defects (see Fig 5). The resulting deficiency of the scalp may be sutured if possible, allowed to granulate or be grafted. Exposure of the tantalum plate must be avoided as it will preclude healing.

5 The use of direct local single or double pedicle flaps has its greatest application in the temporal, parietal and occipital regions. Attention must be directed toward the normal vascular pattern and a wide base is preferred.



A



B



C

FIG 6.—A Hair-bearing scalp in left frontal region from previous débridement with advancement of local flap into defect due to gunshot wound. B Cosmetic restoration achieved by rotation of adjacent scalp flap with application of split-thickness graft to previous hair-bearing area. C Patient with previous hair-bearing scalp in left frontal region prior to discharge.

disfiguring or extremely thinned and adherent, primary revision is preferable prior to cranioplasty. Local frontal pedicle flaps from areas with normal underlying bone may be used in the reconstruction of the eyelids and repaired with a split thickness graft in the presence of a small associated cranial defect. Such a lesion can be repaired easily by entering the previous craniotomy scar and inserting bone if the defect pulsates and by inserting cartilage if no pulsation is present (see Fig 4). In the larger defects where a coronal incision is planned, other provisions for facial repairs must be made to maintain the integrity of the frontal scalp. A contemplated coronal flap should be delayed if there is any doubt about the blood supply in cases where the previous wounds or operations involved the supraorbital vessels.

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Fig 7—Tubed pedicle flap to right frontotemporoparietal area. Dural repair and application of flap accomplished at one procedure; cranioplasty being performed at a later date. Preliminary surgery was done previously at Cushing General Hospital.

4 Relaxing incisions are useful often in small defects (see Fig 5). The resulting deficiency of the scalp may be sutured if possible, allowed to granulate or be grafted. Exposure of the tantalum plate must be avoided as it will preclude healing.

5 The use of direct local single or double pedicle flaps has its greatest application in the temporal parietal and occipital regions. Attention must be directed toward the normal vascular pattern and a wide base is pref

erable to maintain an adequate blood supply. The advantage of the direct flap is that it can be completed usually in one stage.

6 The use of delayed remote flaps is indicated particularly in defects of the frontal region where a local hairbearing scalp flap is obviously unsuited (see Fig 6). Flaps of the latter type were justified during the exigencies of warfare¹ but necessarily must be modified later. Delayed flaps are indicated also in sizable defects which cannot be repaired readily by adjacent scalp tissue.

The undermining of a large remote scalp flap sufficiently to insert and fix a tantalum plate may jeopardize the blood supply, even with good local skin color and without edema unless a considerable period of time has elapsed (see Fig 7). If the flap cannot be reflected safely or adequately bone must be used for the repair instead of tantalum because less exposure is necessary for its insertion. Marginal scars may be entered in approaching the edges of the bony defect. Satisfactory undermining of the flap can be accomplished through these limited incisions. If possible no new incisions should be made through the flap.

If the color of the skin of the pedicle flap over the forehead and face does not match completely that of the adjacent tissues tattooing has given very satisfactory cosmetic results.

COMMENT

The securing of an adequate viable resurfacing of the scalp prior to repair of the bone, dura or brain cannot be overemphasized because deep surgery can be no more successful than surface healing. In some instances closure can be accomplished satisfactorily at the time of cranioplasty or craniotomy. In others preliminary plastic procedures are necessary. If these principles are not observed postoperative necrosis may occur over the plate which occasionally can be closed secondarily.* More often, however infection ensues the plate is removed plastic surgery is completed and the tantalum reinserted at a later date.

SUMMARY

The purpose of this report has been to present the various methods of closure of the scalp. The importance of performing repair of a cranial defect and dura through a good viable scalp flap has been emphasized because primary healing of the surface wound is essential for successful deep surgery. Repair has been achieved by one or more of the following procedures: revision of previous craniotomy scars, relaxing incisions, occasional coronal or craniotomy flaps, split thickness grafts, and local and remote flaps.

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*Harris and Woodhall reported one case in which successful repair of a scalp defect was accomplished by preparing and applying a delayed flap in the presence of an exposed tantalum plate (postoperative necrosis of a thin scalp scar).

CARCINOMA INVOLVING THE COMMON BILE DUCT

REPORT OF FOUR CASES OF SUCCESSFUL RESECTION

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DESPITE the fact that tumors of the common bile duct produce early symptoms and are supposedly late to develop metastases, the ultimate prognosis is still grave in spite of early surgical intervention. Most of these patients eventually succumb to recurrences of the carcinoma, those who survive, ultimately die as a result of the repeated attacks of cholangitis. The avoidance of ascending liver infection which so commonly follows plastic procedures and reimplantation of the common bile duct is an important problem which is yet to be solved.

This paper primarily is concerned with the report of four patients in whom a carcinoma involving the choledochus was successfully resected. In two instances the tumor was so situated that a segmental resection could be carried out, while in the other two cases it was necessary to perform a duodenopancreatectomy.

One can hardly discuss this interesting subject without presenting some of the associated problems that are involved in such surgical procedures.

CASE 1 (Mount Sinai Hospital Admission No. 509702) — Carcinoma involved the junction of the common bile, common hepatic and cystic ducts. Resection of carcinoma with cystic duct and gall bladder and hepaticoduodenostomy were done. The patient was discharged from the hospital improved.

History — D. G. was a 71 year old man who entered the hospital Aug. 24, 1943, complaining of jaundice of four weeks' duration. Family history was irrelevant. Past history disclosed the presence of a mild hypertension for twenty five years with some recent dyspnea on exertion and a prostatectomy four years previously. Otherwise his general health was good until five weeks prior to admission when he noted an icteric tint to the sclerae, light colored stools, and a dark colored urine. The jaundice gradually deepened and with this he noted the onset of postprandial midepigastrie oppression and nausea. As the jaundice became worse, a generalized pruritis developed. There was no pain nor vomiting and weight decreased from 175 to 171 pounds.

Physical Examination — The patient was well developed and nourished, but severely jaundiced. Heart and lungs were normal to auscultation and percussion. The abdomen disclosed a rounded, palpably enlarged mass in the right upper abdomen which moved with respiration. In addition, the liver was distinctly enlarged.

Laboratory Data — Blood pressure was 150 systolic and 70 diastolic in millimeters of mercury. The urine was acid in reaction, specific gravity 1.010, albumin faint trace, sugar negative, bile strongly positive and microscopic normal. The hemoglobin was 80 per cent (Sahli), the red blood cells 4,500,000 per cubic millimeter, the white blood cells 7,400 with a normal differential count. The sedimentation rate was 1 hour and 16 minutes. Urea nitrogen of the blood was 30 mg. per cent, blood sugar was 115 mg. per cent, and the cholesterol of the blood was 565 mg. per cent, the total proteins of the blood were 5.3 mg.

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per cent. The icteric index at first was 36, but the successive blood tests prior to operation showed a steady rise to 60 and then to 80. The serum phosphatase was 46 King Armstrong units per 100 cc of blood. The prothrombin time was 73 per cent of the normal. The blood Wassermann test was negative and the cephalin flocculation test was negative. A scout roentgenogram of the abdomen failed to show any abnormality and radiography of the colon with a contrast barium enema was normal. The electrocardiogram was also normal.

Provisional Diagnosis.—Diagnosis in this case was considered to be a neoplasm involving the common bile duct or head of the pancreas and was based upon the progressive obstructive icterus with the enlarged gall bladder.

Operation.—Operation was performed Aug 31, 1943, under general anesthesia. The procedure carried out was a resection of the gall bladder, cystic duct, portions of the common bile and common hepatic ducts, and hepaticoduodenostomy for a carcinoma situated at the junction of the cystic, common hepatic, and common bile ducts.

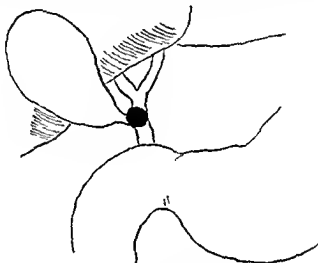


Fig 1—Drawing showing relative position of carcinoma in Case 1

Findings.—There was a firm mass about 2.5 cm in diameter at the confluence of the cystic and common ducts. The distal part of the choledochus was approximately normal in caliber. The common hepatic duct above the tumor was about 1.5 cm in diameter and contained white bile. The gall bladder was markedly distended with white bile, but did not contain any calculi. There were no lymph nodes palpable in the lesser omentum or portal fissure. The liver was dark green in color and careful palpation of its surface failed to disclose any metastases. The common duct and tumor were intimately adherent to the surrounding structures and a number of dilated vessels were present in the lesser omentum.

Procedure.—A right upper rectus muscle-splitting incision was used. After determining the operability of the lesion the distal part of the common duct was freed and a temporary loop was thrown around it. The gall bladder was aspirated and emptied completely. It was then freed from the liver bed subserosally and the cystic vessels were ligated with chromic catgut and then cut. The dissection was continued so as to free the cystic duct completely leaving it and the gall bladder entirely free and hanging attached to the common bile duct and tumor. The common hepatic bile ducts with attached growth were then freed from the surrounding structures in the lesser omentum ligating the dilated surface vessels with fine plain catgut. The distal part of the choledochus was ligated with No. 2 chromic catgut well behind the duodenum and near the upper border of the pancreas following which it was cut across. The entire specimen was then hanging by the common hepatic duct. It was felt

that end to end hepaticocolocholeal anastomosis would have to bridge a gap of almost two inches. Therefore, a hepaticoduodenostomy was decided upon. This was done, first, by placing a posterior layer of fine interrupted linen sutures between the hepatic duct and the duodenum. The duodenum and adjacent hepatic duct were then opened and, using two separate 000 chromic sutures, the inner mucosal layer was sutured using a continuous interlocking suture which was tied at each end. The gall bladder, cystic duct, neoplasm, and segments of the hepatic and common bile duct were removed in one piece by cutting through the anterior wall of the hepaticus. A two-inch long piece of rubber tubing about No. 22 French in caliber was introduced into the anastomosis in such a manner that about one third of its length extended into the hepatic duct and the remaining two thirds protruded into the duodenum. It was anchored in this position with a separate, fine chromic catgut suture. The anastomosis was then completed by the use of a continuous inner Connell type of inversion suture for the anterior liver and then the use of fine interrupted linen sutures for the outer layer. The anastomosis was suspended by placing several fine linen sutures between the duodenum and lesser omentum. A rubber dam drain was placed down to the area of anastomosis and the wound was closed with through and through heavy silk sutures.

Operative Course—The operative course was comparatively uneventful with a minimal temperature rise. A mild bronchopneumonia of the left lower lobe responded rapidly to chemotherapy. There was no biliary leakage from the wound. The jaundice disappeared rapidly and by the eighth postoperative day the stools were brown and the icteric index had dropped to 10 and a few days later to 5. He was discharged from the hospital seventeen days after operation. As far as we know the splinting rubber tube had not been passed.

Gross Pathology—The gall bladder measured 15 by 5 by 3 cm and to it was attached the cystic and part of the common bile duct. The proximal 4 cm of cystic duct was markedly dilated. The distal 2 cm of this duct could not be probed. It was occluded by a firm tumor mass which involved the common bile duct and measured about 2 cm in length. About 2.5 cm of common bile duct were attached to the specimen, of which the proximal part measured 1.8 cm in circumference while the distal part measured 1.3 cm.

Microscopic Diagnosis—Diagnosis was diffusely infiltrating adenocarcinoma originating at the cystic duct orifice infiltrating the common bile duct and causing stricture, hydrops of the gall bladder.

Follow up—The patient was seen about four months after operation and appeared in good health. There was no jaundice and appetite was good. Inquiry two months later disclosed that he had been ill with an episode of chills, fever and some icterus. A report from the family physician stated that the attacks of chills, fever, and jaundice became more frequent the patient went downhill and died at home nine months after operation. Whether this patient had a recurrence of the carcinoma cannot be stated because a post mortem examination was not performed.

CASE 2 (Mount Sinai Hospital Admission No. 523209)—There was a carcinoma of the common bile duct, congenital anomaly of the cystic duct entering the right hepatic duct, and absent common hepatic duct. Resection of gall bladder, cystic, parts of right and left hepatic ducts, and tumor bearing portion of common bile duct was done. Right and left hepaticoduodenostomies were carried out. The patient was discharged from the hospital improved.

History—J. L. was a 50 year old man who entered the hospital July 27, 1944, and was discharged Sept. 11, 1944. Past history was inconsequential. He was perfectly well until about six months prior to admission when he noted the onset of slight nausea and epigastric fullness after meals. Two weeks prior to entry into the hospital he developed some vague upper abdominal pain which was accompanied by jaundice, dark colored urine, anorexia, and constipation. During this period of time he lost approximately ten pounds in weight.

Physical Examination—The patient was thin but showed no signs of emaciation or chronic illness. Skin and sclerae were moderately icteric. Auscultation and percussion of the heart and lungs failed to disclose any abnormality. Palpation of the abdomen

revealed an enlarged liver the free edge extending for two to three fingerbreaths below the right costal margin. The gall bladder was not definitely felt.

Laboratory Data.—The blood pressure was 124 systolic and 44 diastolic in the arms of mercury. Urinal analysis showed no abnormality except for the presence of bile. The hemoglobin was 7 per cent (Sahl) while the white blood cells were 9500 per cubic mm. with a normal differential count. Chemical analyses of the blood showed the following: an albumin of 4.9 gram per cent, urea nitrogen 10.0, total blood proteins 7.3 with the albumin fraction 4.9 and the globulin fraction 2.4; cholesterol was 460 of which the esters were 340 but later the cholesterol rose to 1010 with the esters 480. The atherogenic index was at first 49 but then rose to 60. The galactose tolerance test was normal and the cephalin flocculation test rose from 1 to 4+. Electrocardiograms of the heart were normal. Cystic tests of the stools were negative for bile. Roentgenograms of the gastrointestinal tract were normal.

Postoperative Note.—It was found that the patient had a bilious carcinoma which was probably caused by a neoplasm of the stricture in the. Exploratory laparotomy was instituted.

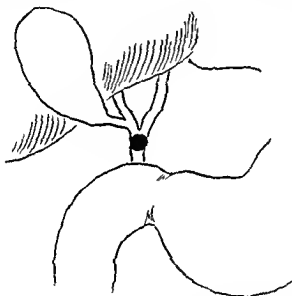


Fig. Diagram showing the position of the biliary ducts and carcinoma in Case 4.

Operation.—Operation performed under ethylene and nitrous oxide on Aug. 10, 1944. The gallbladder and excised were the site of the portions of the common bile duct and right and left hepatic ducts. A neoplasm of the common bile duct. Right and left hepaticoduodenostomy and anastomosis jejunostomy for alimentary anastomosis were done.

Findings.—There were adhesions between the right lobe of the liver and diaphragm which completely obliterated the right subphrenic space. The gallbladder was markedly distended. In the region of the portal fissure a large distended bile duct was visible. It was about 3.5 cm. in diameter and later a transverse section was proved to be a markedly dilated left hepatic duct. About 1 m. distal to the area a firm regular nodule about 1 cm. in diameter felt as though to be a neoplasm. The second part of the duodenum was situated close to the lower of the liver. Distal to the nodule the common bile duct was found to be situated deeply in the lesser omentum about 2½ cm. in diameter and covered by a number of dilated venoles and bands. The right duct emptied into the distal part of the right hepatic duct which was about 1 to 1½ cm. in diameter. The left hepatic duct was about 2 to 2.5 cm. in diameter. The gallbladder and hepatic ducts were filled with a thick yellow green bile. The tumor was situated in the common bile duct just

distal to the junction of the right and left hepatic ducts. There were no metastatic nodes in the liver nor in the portal fissure area.

Procedure.—A right upper rectus muscle splitting incision was used. After opening the peritoneum and dividing the local adhesions, it was felt that the lesion could be resected. The dilated veins and bands overlying the distal common bile duct were doubly ligated with fine plain catgut and divided. A temporary loop was thrown around the common bile duct and separated from the liver bed. No. 2 chromic catgut and cut. The cystic duct was then freed and mobilized to its junction with the right hepatic duct. The distal common bile duct was then doubly ligated with No. 2 chromic catgut and divided. Using the proximal end of the choledochus as a tractor, the rest of the common duct together with the tumor and the right and left hepatic ducts were completely mobilized so that the gall bladder, and cystic and tumor-bearing part of the choledochus were hanging by the two hepatic ducts. Because of the position of the growth and the unusual anomaly of the cystic duct no other procedure for restitution of the biliary flow was feasible except for a separate right and left hepaticoduodenostomy. This was done by placing several interrupted 000 chromic catgut sutures between the posterior walls of the two hepatic ducts and the second part of the duodenum. The two anastomoses were separated by a distance of almost 1 cm. Following this the posterior walls of the right and left hepatic ducts were cut across transversely and the adjacent parts of the duodenum were opened. A second posterior layer of 000 chromic catgut was then placed in each anastomosis and this suture passed through all the coats of the duodenum and ducts. The specimen was then removed by cutting through the anterior walls of the two hepatic ducts. The two inner layers were completed anteriorly by the use of a Connell inversion suture after placing a No. 20 French size piece of rubber tubing two inches in length in each anastomosis so that about two thirds of the tube protruded into the duodenum. These tubes were anchored in position by a separate single fine chromic catgut suture. A second layer of 000 chromic catgut interrupted sutures was then placed between each duct and the duodenum. The anastomosis was supported by placing a few fine sutures between the duodenal wall and the capsule of the adjacent liver.

Because of the two anastomoses it was considered advisable to do a Stamm-Kader type of jejunostomy about sixteen inches distal to the ligament of Treitz using a No. 16 French whistle tip catheter. This was brought out through a separate left lateral stab wound. Two rubber dam drains were placed down to the anastomoses and the abdomen was closed in layers with No. 2 chromic catgut and several reinforcing heavy silk sutures which were passed through all the layers of the abdominal wall. The patient was given a transfusion of 500 cc of citrated blood during the operation.

Postoperative Course.—Within a few hours after operation, bile was noted in the stomach contents which were aspirated through the nasogastric Levine tube. During the first twenty-four hours fluids were administered by a continuous slow drip intravenous infusion of glucose in saline solution. Following this, nutriment, fluids, vitamins, and other substances were given through the jejunostomy tube. The same falcium mixture was administered through the jejunostomy that has been used on the Service for jejunostomy alimentation in non-gastrointestinal patients. On the fifth postoperative day some biliary drainage was noted on the dressings, but the wound healed by primary union. On the twenty-first day the temperature rose to 102° F and this coincided with the cessation of the biliary leak. It was felt that this fever was due to cholangitis and it subsided after several days with the administration of sulfadiazine. A mild secondary anemia was treated with iron preparations and transfusion of citrated blood. The jejunostomy tube was removed on the fourteenth day and all feedings were given orally. On the sixth day after operation the icteric index had dropped to 15 and one week later a test of the icteric index showed it to be 6. The patient was discharged from the hospital Sept. 11, 1944, which was thirty-two days after operation. At this time his weight was 112½ pounds as compared with a preoperative weight of 113 pounds. This maintenance of weight was thought to be the result of early feeding by jejunostomy.

Gross Pathology—The specimen consisted of a gall bladder with about 3.5 cm of common bile duct. Attached to the common duct were about 8 mm of right and left hepatic ducts which were markedly dilated. Immediately below the bifurcation of the hepatic ducts there was a hard mass within the common bile duct which on section revealed a completely encircling grayish white, soft tumor about 1 cm in length. The lumen was almost obliterated. The gall bladder was markedly distended with greenish bile, but did not contain calculi. The cystic duct entered the right hepatic duct.

Microscopic Diagnosis—Diagnosis was adenocarcinoma of the common bile duct and anomalous opening of the cystic duct into the right hepatic duct.

Follow-up Course—On leaving the hospital the patient was asked to return to the follow up clinic three months later. He sent a card stating that he was ill with chills and fever. We were unable to examine him at any subsequent time because it was reported that he died at home nine months after operation. Inquiry from the family physician resulted in the information that in the last few months he suffered from recurrent chills, fever, jaundice, and loss of weight. No post mortem examination was obtained, but the clinical picture suggests recurrent cholangitis with perhaps a return of the original carcinoma.

CASE 3 (Mount Sinai Hospital Admission No 499047)—There was an adenocarcinoma of the lower end of the common bile duct. Resection of the head of the pancreas duodenum and terminal common bile duct and cholecystogastrostomy, gastrojejunostomy, and complementary jejunostomy were done in one stage.

History—L. Z. was a 56 year old, married woman who entered the hospital Dec 12, 1942, and was discharged on Feb 18, 1943. She was operated upon Dec 17, 1942. Past history disclosed that a vaginal plastic operation was done five years previously and that one year before admission she

160 mm of mercury regime without the months before hospitalization with a generalized pruritus which was followed shortly after by distinct icterus, light colored stools, and a dark urine. During this period she lost approximately thirty pounds in weight, and noted a sense of fullness in the right hypogastrium.

Physical Examination—The patient was thin, somewhat emaciated, and slightly icteric. Auscultation and percussion of the heart and lungs failed to disclose any abnormality. The abdomen was scaphoid and in the right upper quadrant the liver could easily be felt extending about two fingerbreadths below the costal margin. In addition, a globular mass interpreted as being a distended gall bladder was also noted. No other abnormal findings were found in the remainder of the physical examination.

Laboratory Data—Urinalysis was normal except for a trace of bile. The blood count showed a hemoglobin of 90 per cent (Sahli) with normal white blood cell and differential counts. The blood Wassermann test was negative. Chemical analyses of the blood in milligrams per cent showed the following: urea nitrogen 13.0, sugar 100, cholesterol 480 with the ester fraction 300, total proteins 6.2 of which the albumin fraction was 4.3. The xerens index was 5, on the first examination, but then rose to 12. The serum phosphatase (alkaline) was 33 King Armstrong units and the cephalin flocculation test was negative. Guaiac tests of the stools were negative for blood.

Preoperative Diagnosis—The enlarged gall bladder and history of jaundice which waxed and waned suggested the possibility of a neoplasm at the ampulla of Vater. Common duct calculus could not be excluded.

Operation—Exploratory laparotomy was performed* under continuous spinal anesthesia Dec 17, 1942. A one-stage operation was done consisting of a resection of the head of the pancreas, duodenum (first and second parts) and terminal common bile duct with restoration of continuity by a cholecystogastrostomy and a posterior gastrojejunostomy. The pancreatic ducts were ligated and a complementary jejunostomy was done.

*By Dr Ralph Cole

Findings—The gall bladder and common bile duct were markedly distended with greenish yellow bile. The liver was distinctly enlarged and icteric in appearance. After partly mobilizing the second portion of the duodenum, a tumor nodule about 1 cm. in diameter was felt behind the duodenum in the general region of the papilla. This mass was considered to be a neoplasm which, because of its mobility and the absence of metastases, was suitable for resection.

Procedure—A right upper rectus muscle splitting incision was used. After opening the peritoneum and evaluating the pathology, the gall bladder was emptied by aspiration for a better local exposure. The duodenum and head of the pancreas were mobilized by cutting the peritoneal attachment on the outer border. The common bile duct was isolated in the lesser omentum and a loop was thrown around it. The duodenum was then cut across between clamps at the junction of the second and third portions and the distal end was closed with a double layer of sutures using 0 chromic for the inner layer and a continuous fine linen suture for the outer layer. The stomach was then cut across just proximal to the pylorus after ligating the right gastric and gastroduodenal vessels with linen ligatures. A retrocolic two layered gastrojejunostomy was then performed (side-to-side) using a continuous 0 chromic catgut suture for the inner layer, going through all coats of the stomach and jejunum, and

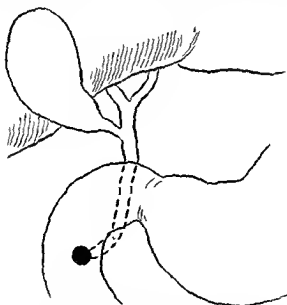


FIG. 3.—Diagram showing position of carcinoma in Case 3.

then using a fine linen suture going through the seromuscular coats for the outer layer. The common bile duct was then doubly ligated with fine linen ligatures and cut across after which the pancreas was divided between its head and neck identifying the dilated pancreatic duct which was separately ligated with linen. The pancreatic stump was sutured with several interrupted fine linen stitches. Biliary alimentary flow was re-established by anastomosing the gall bladder with the ant. pyloric end of the stomach by means of a two layered suture anastomosis. About sixteen inches distal to the gastroenterostomy, a Stamm-Käfer type of jejunostomy was done using a No. 16 French whistle tip catheter which was then brought out of the abdomen through a separate left lateral stab incision. The stump of the pancreas was drained with a piece of rubber dam and the abdomen was closed in layers using No. 2 chromic catgut and, in addition, several heavy silk sutures were used to reinforce the wound by passing them through all the layers of the abdominal wall. During the operation, a transfusion of 500 cc. of citrated blood was administered intravenously by slow drip.

Postoperative Course—The patient did fairly well after operation. At no time was there any evidence of shock. The highest rise in temperature was up to 102.5° F., which gradually subsided. Intravenous fluids were administered by drip method for the first twenty-four hours following which the nutritional and fluid balance were maintained by the feeding of a pabulum mixture and other fluids through the jejunostomy tube. On the tenth post-operative day a pancreatic fistula was in evidence and was proved by the demonstration of diastase enzymes in some of the aspirated fluid. The fistula discharged several hundred cubic centimeters daily and gradually diminished until a complete stoppage occurred about one month after operation. At no time were there any signs of steatorrhea. Just at the time that the pancreatic leakage ceased, a mild biliary fistula appeared which closed spontaneously after fourteen days. The patient was discharged from the hospital Feb. 18, 1943 which was sixty-three days after operation.

Gross Pathology—Specimen consisted of a resected portion of duodenum together with a portion of common bile duct and a portion of the head of the pancreas. The duodenum measured 8.5 cm. in length and 3 cm. in diameter. The wall was thin and the serosa smooth. The papilla of Vater was located 1.5 cm. from the distal line of resection. The walls of the papilla were considerably thickened and firm in consistency. Just below the papilla, the duodenal mucosa was elevated, firm, and eroded for about 0.5 cm. The common bile duct was dilated to 1.5 cm. in diameter and was 6 cm. in length. The wall was thin. Distally, the common bile duct was obstructed by a firm nodule 1 by 0.5 cm. in width, which was located beneath the mucosa of the papilla of Vater. The portion of pancreas measured 3 cm. in width and 1 cm. in length. The pancreatic duct was dilated.

Microscopic Diagnosis—Diagnosis was infiltrating adenocarcinoma originating in the common bile duct at the papilla of Vater. Pancreas showed marked lipomatous and was not involved by carcinoma.

Follow-up Course—June 16, 1943, the patient felt fairly well although she had not gained any weight. This was recorded as being 104 pounds. There were no chills, fever or jaundice. Appetite was poor and the stools were not bulky.

October 29, 1943, she was readmitted to the hospital because of loss of weight, chills, fever, and acholic stools. Examination disclosed some tenderness in the right upper abdomen. The white blood cells were 21,700 per cubic millimeter with 90 per cent polymorphonuclear leucocytes. Hemoglobin was 65 per cent (Sahli). General appearance was that of a chronically ill woman. Treatment consisted of forced feeding and sulfadiazine therapy which caused a subsidence of the fever. She was discharged from the hospital with a diagnosis of ascending cholangitis.

March 15, 1944, the weight was 93 pounds. There was a mild degree of icterus. The liver was notably enlarged and smooth. Bowels moved once daily were not bulky and were brown in color.

June 5, 1944, the patient complained of weakness and swelling of the abdomen. Weight was recorded as 100 pounds and the increase over the previous reading was undoubtedly due to the accumulation of fluid in the abdomen and tissues. Paracentesis abdominis was performed, removing 2,500 cc. of amber colored ascitic fluid. Examination of this fluid failed to show tumor cells. It was considered that she was probably suffering from a recurrence of the carcinoma with involvement of the portal fissure and portal obstruction.

June 29, 1944, the patient was readmitted to the hospital in a distinctly cachectic state. The abdomen was enlarged and filled with fluid. The sclerae were icteric. After paracentesis of the abdomen was done the liver was found to be considerably enlarged and nodular. It was obvious that there were multiple metastases to the liver with portal vein obstruction. She gradually went downhill and died July 9, 1944 which was nineteen months after operation. Post mortem examination was not permitted.

CASE 4 (Mount Sinai Hospital Admission No. 57-240)—There was adenocarcinoma of the head of the pancreas with stenosis of the common bile duct. Excision of the pyloric end of the stomach, first, second, and part of the third portion of the duodenum, lower end of the common bile duct and head of the pancreas was done. Reconstitution of continuity by antecolic

terminolateral gastrojejunostomy and cholecystojejunostomy was carried out, and exclusion of the external pancreatic secretion by ligation of the pancreatic ducts

History—J S, a 59 year old married woman, was admitted to the hospital March 21, 1945. Past history was irrelevant. She had enjoyed good health until six weeks prior to admission, when she noted for the first time some epigastric fullness and distress after eating some cheese. This was followed by nausea and vomiting which lasted for about twenty four hours. Shortly thereafter she noted the onset of anorexia, light colored stools, and a dark urine. Noticeable jaundice then became evident which steadily increased in intensity and was accompanied by a generalized pruritus. During this period she lost twelve pounds in weight.

Physical Examination.—The patient was well developed and nourished and moderately jaundiced. The lungs were normal to auscultation and percussion. The heart was somewhat enlarged to the left and the heart sounds were poor in quality. The blood pressure was 112 systolic and 70 diastolic, measured in millimeters of mercury. The abdomen was obese and palpation disclosed the liver to be enlarged to a point of four fingerbreadths below the right costal margin. In addition a definite smooth rounded mass was felt beneath the liver which moved with respiration. This was considered to be a distended gall bladder. Rectal and vaginal examinations disclosed no abnormality.

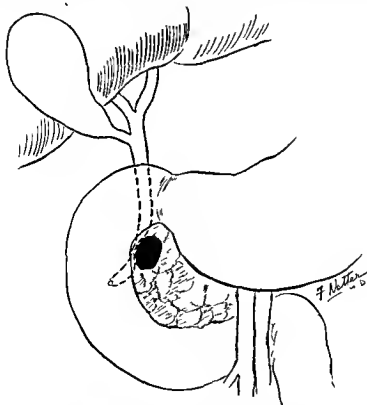


Fig 4.—Diagram showing position of carcinoma in Case 4

Laboratory Data—Urinalysis was normal except for the presence of considerable bile. Chemical analyses of the blood yielded the following results in milligram per cent: urea nitrogen was 80, cholesterol was 330 with the ester fraction 225, total proteins were 7.4 with the albumin fraction 4.3 and the globulin component 3.1. Sclerotic index was 30. The blood Wassermann test was negative. A routine roentgenogram of the abdomen was negative except

for the presence of a rounded shadow in the right upper quadrant which was presumed to be an enlarged gall bladder. The electrocardiogram showed evidence of an atypical right bundle branch block and myocardial damage.

Preoperative Diagnosis—The insidious onset of gradually deepening icterus with an enlarged gall bladder suggested a diagnosis of neoplasm involving the lower end of the common bile duct or head of the pancreas.

Operation—Operation was performed under ethylene and ether anesthesia on March 26, 1945. Resection of the pyloric end of the stomach, the first, second and part of the third portions of the duodenum and the head of the pancreas for a neoplasm of the head of the pancreas which obstructed the common bile duct was done. Continuity was restored by an antecolic terminolateral gastrojejunostomy (Polva type) and a choledochostomy. The pancreatic ducts were ligated.

Findings—The gall bladder was markedly distended with yellow bile. The liver was enlarged and icteric. There were no metastatic nodules on palpation of its surface. The common bile duct was dilated to approximately 2.5 cm. in diameter. Situated in the upper border of the head of the pancreas was a hard mass about 3 cm. in diameter. The tumor was freely movable, but constricted the pancreatic part of the common bile duct, and on its deep surface was somewhat adherent to the termination of the superior mesenteric vein. The duodenum itself was not invaded and there was no evidence of regional lymph enlargement.

Procedure—A right upper rectus muscle-splitting incision was used. After opening the peritoneum and exploring the biliary tract area, the gall bladder was emptied by aspiration for a better local exposure. The patient took the anesthesia poorly and the anesthetist consistently called attention to the variable quality of the pulse advising that further operative procedure be planned so that the operation could be terminated within a short time if necessary. The common bile duct was freed from its bed in the lesser omentum and a temporary loop was thrown around it. The duodenum was mobilized from its bed together with part of the adjacent pancreas by incising the peritoneum on its outer border. The right gastric and gastropiploic vessels were ligated and cut so as to free the pyloric end of the stomach. The mobilization was completed except for the point of adherence of the tumor to the superior mesenteric vein. The duodenum was then transected through its third portion between Payr clamps and the distal end was closed using two separate continuous inversion sutures of fine linen. The pancreas was then incised at the junction of the head and neck, identifying the dilated pancreatic ducts and clamping a few small bleeding areas on its cut surface. The specimen was then turned upward to expose the superior mesenteric vein and the adherent portion of the tumor was freed from the vein with the point of the scalpel. The stomach was then cut across several centimeters from the pylorus and the specimen was removed by doubly ligating the dilated common bile duct with heavy linen ligatures and cutting the duct distal to them. The pancreatic ducts were then ligated by the use of two separate mattress sutures of linen which were passed around the ducts and tied. The pancreatic stump was then closed with several fine linen stitches. An antecolic terminolateral gastrojejunostomy (Polva type) was next performed using a two-layered suture type of anastomosis with a chrome catgut for the inner and fine linen for the outer layer. Several inches distal to the anastomosis and making a stoma approximately 3 cm. in width a choledochostomy was done again using a two-layered suture anastomosis. A rubber dam drain was inserted down to the pancreatic stump and was brought out through a right lateral stab wound. The abdomen was closed in the usual manner.

Postoperative Course—The postoperative course was reasonably smooth. The highest temperature rise was 101.8° F., which subsided after several days. On the third day after operation, some biliary drainage was noted on the dressings. It was never profuse and stopped completely after five weeks. Stools were definitely brown on the tenth day. Fluids were given intravenously for seventy-two hours after which nutrition and fluids were given

per os. A mild superficial separation of the wound was noted on the twelfth postoperative day. This was treated by packing, with resultant granulation and subsequent healing. She was discharged from the hospital May 7, 1945 which was forty-two days after operation.

Gross Pathology.—The specimen consisted of the terminal end of the stomach, common bile duct, duodenum, and a portion of pancreas. The pyloric region measured 4.5 cm., and the duodenum 11 cm. in length. Attached were a segment of pancreas measuring 6.5 cm. and 8 cm. of common bile duct. The latter was dilated to a circumference of 3 cm. The portions of stomach and duodenum were normal and the papilla of Vater was likewise normal. Beginning at a point 1.5 cm. from the proximal end of the choledochus, the duct became markedly narrowed and puckered for a distance of 3 cm. by a tumor mass in the pancreas which infiltrated the wall of the common bile duct. This tumor was about 3 cm. in diameter and occupied the portion of the pancreas near the common duct. The undersurface of the pancreas was roughened. A dilated pancreatic duct about $\frac{3}{4}$ cm. in diameter was identified and could not be probed. Distal to the tumor, the common bile duct appeared normal down to the ampulla of Vater.

Microscopic Diagnosis.—Diagnosis was scirrhous carcinoma of the head of the pancreas with invasion and constriction of the common bile duct.

Follow up Data.—June 12, 1945, the patient appeared at the office. She appeared somewhat pale and complained of a poor appetite and weakness. Bowels moved once daily, were brown in color, and not bulky. She was advised to go to a convalescent home.

July 23, 1945, she had developed, about one week before, marked weakness, chills, fever up to 105° F., and some jaundice. In addition there had been a slow decrease in weight. She was readmitted to Mount Sinai Hospital where examination revealed a moderately icteric, pale chronically ill woman. There was a marked edema of the lower extremities. Fever ranged between 100 and 103° F. The hemoglobin was 51 per cent (Sahli). The total proteins of the blood were 4.1 mg. per cent with the albumin fraction 1.9 and the globulin 2.2 mg. per cent. The cephalin flocculation test was 3 plus (the xero index 21), and the cholesterol of the blood 260 mg. per cent, of which the ester fraction was 120 mg. per cent. During her stay in the hospital in the succeeding weeks the fever and chills recurred, at no time could it be stated that the administration of sulfadiazine or penicillin altered the clinical picture. The abdomen revealed evidence of ascites and the edema of the lower extremities persisted. This was partly attributed to the low plasma proteins. There was no evidence of metastases in the liver, but this obviously could not be excluded. She was discharged from the hospital on Sept. 1, 1945 with the condition unimproved.

She was not heard from since that time but the family physician reported that she died at home during the early part of November 1945. Undoubtedly, the terminal course of events was due to metastases to the liver with repeated cholangitic attacks.

DISCUSSION

In the past decade renewed efforts have been directed toward eradication of neoplasms involving the common bile duct and pancreas. The difficulties involved in mastering this complicated problem are gradually being overcome by the progressive development of surgical technique and a better understanding of the importance of biliary secretion and pancreatic enzymes. As a result of the many animal experiments and the various experiences with operations in the human being surgical procedures involving the pancreas and common bile duct are now being done with less timidity, with more success, and with a lower mortality rate than in former years due in part to the use of vitamin K, antibiotics, the sulfonamide drugs and the maintenance of electrolytic balance.

Historical Background.—According to Mayo Robson, the first case of carcinoma of the ampulla of Vater was described by McNeil in 1835, and in 1840

Durand Fardel described the first case of carcinoma of the common bile duct late in the nineteenth century, Von Vering and Minkowski demonstrated that removal of the pancreas in dogs led to the development of diabetes. It was not until 1921 that Banting and Best were able to isolate the active principle from the pancreas which controlled the sugar metabolism in diabetes.

In the field of surgery we find a report of the removal of a tumor from the body of the pancreas by Trendelenburg in 1882 and mention of the supposed extirpation of the entire pancreas in man by Billroth in 1884. According to Sauvé, resection of the head of the pancreas had been performed at least seven times by 1898. The operation by Codivilla in the same year is of interest. He resected the head of the pancreas, duodenum, pyloric end of the stomach and at the same time re-established continuity by a Roux type of gastroenterostomy and a Murphy button choledochenterostomy (Trimble and associates). Although his patient died twenty four days after operation due to cachexia and diabetes, the surgical procedure heralded by many years the operation of today. Also in 1896 Halstead resected a neoplasm involving the papilla of Vater with reanastomosis of the pancreatic and bile duct to the duodenum. His patient survived for seven months. Apparently Ulizowski in 1902 was the first surgeon to perform a segmental resection of the common bile duct for carcinoma but he failed to re-establish biliary intestinal continuity and his patient died three days later. The following year Kehr successfully removed a neoplasm of the choledochus and at the same time anastomosed the hepatic duct with the duodenum. His patient survived for twenty seven months. Sauvé in 1909 as a result of studies on the cadaver advocated removal of the head of the pancreas by a two stage operation. The first step called for a gastroenterostomy and for the second stage he advised resection of the second portion of the duodenum adjacent pancreas and choledochenterostomy. He predicted a lower incidence of cholangitis with choledochointestinal anastomoses than in instances where the gall bladder was used. He also advised against pancreaticenterostomy and advocated drainage of the pancreatic stump. In the recent article by Whipple, Hauech in 1912 carried out the first successful partial pancreaticoduodenectomy in two stages implanting the stump of the resected pancreas into the distal end of the resected duodenum. His patient survived for nine months and developed an acute cholangitis. Autopsy revealed no metastases or recurrences. He also mentioned the report of Hirschel in 1914 who performed a resection of part of the duodenum and pancreas, a choledochoduodenostomy and an implantation of the pancreatic duct with survival of the patient for one year. Likewise the successful two stage operation of Tenam in 1922 is quoted. He implanted the stump of the pancreas into the duodenum after resection of an ampullary growth and the patient was well three years after operation. Considerable credit must be given to Whipple for his reawakening an interest in duodenopancreatectomy. With his associates in 1935 a two stage operation was advocated for removal of ampullary carcinoma with exclusion of the pancreatic secretion. The first successful radical pancreaticoduodenectomy for carcinoma of the pancreas should be credited to Brunschwig in 1937. Three

years later Whipple and, almost simultaneously, Trimble and associates reported the successful results of a one-stage operation and emphasized the advantage of such a procedure

Numerous modifications have been suggested for duodenopancreatectomy and especially in the treatment of the pancreatic stump and the re establishment of biliary intestinal continuity Whipple discarded the earlier suggestion of anastomosis of the gall bladder directly to the stomach or intestine for a choledochojunostomy of the Roux type This was to avoid biliary leakage from the heated common duct stump and to minimize the postoperative incidence of cholangitis Brunshaw utilized a loop of jejunum for a cholecystojejunostomy with a distal jejunojejunostomy Trimble implanted the proximal common bile duct into the jejunum through a stab wound in the bowel Pearse in his one stage duodenopancreatectomy restored the biliary and digestive tract continuity with only two anastomoses one between the end of the jejunum and the gall bladder and the other between the cut end of the stomach and the more distal side of the jejunum Cole suggested a Roux type of choledochojunostomy with the formation of valve-like indentations in the jejunum distal to this anastomosis to prevent reflux of the intestinal contents into the biliary tree

In the last two cases reported by Child he performed a duodenopancreatectomy and anastomosed the pancreatic stump with the open end of the jejunum more distally sutured the choledochus to the jejunum end to side and still lower down made an end to side gastrojejunostomy In 1946 Whipple advocated anastomosis of the pancreatic duct with the jejunum through a goiter tube

Incidence—As emphasized by Cohen and Colp tumors of the lower end of the choledochus are intimately related to neoplasms arising from the papilla of Vater and the head of the pancreas They stated that carcinoma of the ampullary region may arise either from the intestinal epithelium of the papilla, from the termination of Wirsung's duct or from the mucosa of the lower end of the bile duct Carcinomas originating from the choledochus in the papillary area are four times as frequent as those developing from the pancreatic duct It has been generally estimated that common bile duct cancer occurs in from 3 to 3.6 per cent of all patients succumbing to malignancy Kirschbaum and Kozoll in 13,300 autopsies at the Cook County Hospital found 1,808 cases of malignant tumors of which 62 were due to carcinoma of the bile ducts (3.4 per cent) In another series of 4,239 autopsies at the Glasgow Royal Infirmary, quoted by Packard and Blalock there were 18 instances of cancer of the bile ducts Renshaw mentioned the series of 4,578 necropsies by Kellynack with only 2 cases of bile duct cancer and also stated that he was able to find 20 instances of primary duct carcinoma in the records of the Mayo Clinic between the years of 1907 and 1921

The distribution of the primary lesion within the bile ducts is of some interest Rolliston and McNee in a series of 92 cases of extrahepatic biliary duct carcinoma reported the following: 23 lesions arose in the hepatic ducts, 6 in the cystic duct, 28 at the junction of the cystic, hepatic, and common bile ducts, and

35 in the common bile duct proper Kirschbaum and Kozell in their series of 62 cases report 7 cases in the cystic duct 13 in the hepatic ducts 32 in the *choledochus* and 10 cases in the papilla of Vater Marshall's series shows a high incidence of ampullary lesions

Pickrell and Blalock enumerated 22 instances of resection of the common bile duct for carcinoma They failed to mention the case of Moschowitz 14 to 1921 Cohen and Colp were able to collect 58 cases of neoplasms involving the papilla of Vater where surgical removal was carried out This series of cases was increased to 124 in the report by Hunt in 1941 Between 1930 and April 1942 Whipple collected 64 cases of radical pancreaticoduodenectomy of which 23 cases alone were reported within the year preceding 1942 By December 1944, the same author quoted Orr as having collected 104 cases of radical resections for carcinoma of the ampulla and ampullary region

These figures serve to indicate that surgeons have lost their timidity in operating for neoplasms involving this hitherto "untouchable" area

Pathology—A classification of the histologic types of carcinoma is given by Kirschbaum and Kozell in their series of 62 cases

Common bile duct The commonest type of tumor was an infiltrating adenocarcinoma Less common were the papillary adenocarcinoma and the medullary carcinoma

Papilla of Vater The majority of the neoplasms were papillary adenocarcinomas while the other two types were the infiltrating adenocarcinomas and the squamous cell carcinomas

The usual cell in these tumors is cylindrical (Renshaw) although spheroidal and mucous cell types can occur Mucous producing carcinomas are more frequent in the gall bladder than in the ducts Squamous cell neoplasms are obviously the result of metaplasia

The papillary adenocarcinomas are supposed to result from malignant transformations of a benign polyp These occur both in the gall bladder as well as in the bile ducts and may be pedunculated They produce obstruction by projecting into the duct lumen in papilla of Vater in the same mechanical manner that a stone or foreign body may obstruct Essentially they are as malignant as the infiltrating adenocarcinomas which cause biliary obstruction by the formation of a local stricture Finally the biliary flow may be blocked by the pressure of metastatic lymph nodes

The lymphatic spread of carcinomas of the bile duct may involve (1) the sentinel lymph node at the termination of the cystic duct (2) lymph nodes in the porta hepatis (3) periductal (4) peripancreatic and (5) periaortic nodes Metastases may also develop in the liver and more distant areas

Curiously metastases from *choledochal malignancies* are supposed to occur late Thus Renshaw quoted Davis and Goltzstein who found an incidence of 20 per cent in their series of common duct neoplasms Pickrell and Blalock mentioned the report of Diek who in 13 autopsy cases of cancer of the *choledochus* found no extension of tumor beyond the wall of the duct in 11 cases and no secondary deposits in the lymph nodes They also quoted the report of

Marshall who found metastases in only 12 out of 49 instances of extrahepatic biliary duct carcinoma. Cohen and Colp stated that in 4 of the cases of papillary cancer that were autopsied at The Mount Sinai Hospital there were no evidences of metastases. The latter authors also quoted Perry and Shaw who noted metastases in only 3 out of 15 instances of papilla carcinoma. On the other hand Kirschbaum and Kozoll reported an incidence of 76.7 per cent metastatic lesions in their series of 62 autopsied cases of bile duct carcinoma.

In contrast with gall bladder neoplasms ductal malignancy is less frequently associated with evidences of cholecystitis or cholelithiasis. This undoubtedly explains the high incidence of distended gall bladders in common bile duct neoplasms.

Other associated pathologic lesions may be present. These are largely the result of biliary obstruction and infection. Within the liver one may find biliary cirrhosis, cholangitis and liver abscesses. Bile peritonitis has resulted from perforation of the gall ducts and bladder or is due to a transudation from the markedly distended and obstructed biliary tree. Ascites can occur as a result of peritoneal implants while occlusion of the pancreatic ducts may cause atrophy of the pancreas and fat necrosis.

Physiologic Alterations—Tumors involving the common bile duct and adjacent head of the pancreas and duodenum are expected to produce major changes in function. These may be divided into hepatic, pancreatic and alimentary groups.

Liver—Interference with biliary flow causes dilatation of the biliary tree and bile radicals of the liver. The resultant icterus and the frequent concomitant infection leads to necrosis of liver lobules and infiltration of the periportal areas with inflammatory cells. The icteric index rises, the Van den Bergh test becomes promptly positive and the body tissues become stained with biliary pigments. The various liver function tests (bromsulfalein, cephalin flocculation, etc.) show evidence of hepatic impairment. Elimination of bile from the intestinal tract causes light colored stools and poor fat absorption from the bowel. Distention of the biliary tree may cause not only a loss of appetite but pain which varied from mild epigastric distress in 11 cases to severe biliary colic.

Pancreas—Obstruction of the external pancreatic secretions implies complete occlusion of Wirsung's duct and the accessory duct of Santorini. The average amount of pancreatic juice which enters the intestine varies from 500 to 800 cc daily. In one case of external pancreatic fistula due to a pancreatic cyst over 1770 cc were recovered in twenty-four hours (Miller and Wiper). Since this patient's stools and intestinal digestion were undisturbed it must be assumed that some pancreatic juice must have entered the intestine. The external secretion of the pancreas contains the proteolytic enzyme trypsinogen which is activated by the intestinal enterokinase, the carbohydrate splitting enzyme amylase and the fat splitting enzyme lipase which is enhanced in action by the presence of bile. Obstruction of the pancreatic ducts by a neoplasm should lead to loss of enzymatic action and intestinal digestion. This theoretical expectation has not been borne out in the studies of patients who were subjected

to duodenopancreatectomy with exclusion of the pancreas. Thus, in two of Whipple's cases, about 85 to 90 per cent of the ingested fat was absorbed. He suggested the possibility of an additional fat splitting enzyme in the intestine. It is also possible that some physiologic adjustment has occurred in these patients because a certain amount of acinar atrophy within the pancreas had already taken place prior to operation.

One may mention that even those patients who were subjected to total pancreatectomy do not necessarily exhibit alterations in food digestion although these cases develop diabetes.

Considerable discussion has arisen regarding the relationship of loss of external pancreatic secretion and the development of fatty infiltration of the liver and a lowered blood lipid content. Animal experimentation with ligation of the pancreatic ducts and complete depancreatization in dogs maintained on an adequate diet and insulin have shown the following: (1) The fat content of the liver increases 20 or more per cent. This is not evenly distributed throughout the liver and does not occur until twelve to twenty-four weeks after operation. (2) The blood lipid level drops and the esterized cholesterol fraction may disappear (Montgomery, Entenman, Chaikoff, Kaplan, Allan, Bowie, MacLeod, and others). These effects are not related to the amount of fat intake (Bloor). The ingestion of fresh pancreatic juice, raw pancreas, lecithin, choline, and lipocaine as suggested by Dringstedt prevents the lowered blood lipids and fatty liver. Also the administration of these factors will reverse the fatty changes in the liver. It has also been shown that if depancreatized dogs live long enough there is a spontaneous regression of the fatty liver. Although Dringstedt suggested lipocaine as an internal secretion or hormone of the pancreas, various experimenters have brought evidence in apparent contradiction.

From a practical standpoint it can be stated that some patients in whom the external pancreatic secretions are excluded will tolerate and digest food and fats well while others derive benefit from lipocaine and adjuvant pancreatic extracts. The experimental work in dogs has not been completely borne out in man regarding the effects of total pancreatectomy and exclusion of the external pancreatic secretions. Fatty infiltration of the liver was found at autopsy in 10 out of 52 cases of carcinoma of the pancreas and ampulla by Schnedorf and Orr. The blood lipids in man have not been altered in some of the cases of total pancreatectomy and occlusion of the external pancreatic secretions. Perhaps the diet contained adequate amounts of lipocaine or lecithin.

Alimentary.—Duodenal obstruction can occur in neoplasms involving the head of the pancreas. In such instances the clinical picture is similar to that of pyloric obstruction with the evidences of vomiting, loss of appetite and weight, loss of chlorides and its secondary effects. Radiography of the stomach and duodenum may reveal distention of the duodenum and stomach while on occasions the duodenal curve is distinctly widened.

Clinical Features.—Many of the clinical features have already been mentioned. The classical clinical picture of carcinoma of the duodenum or papilla or adjacent head of the pancreas is generally characterized by a progressively

deepening and painless jaundice which is associated with an enlarged and palpable gall bladder. Symptoms usually appear early due to the strategic location of the neoplasm. The history is frequently of short duration. Pain may vary from a dull epigastric distress to severe biliary colic. The icterus is progressive and the stools become acholic. In the group of 222 cases studied by Laeher Stewart, and Lund jaundice was present in all but four of the patients. Melena is uncommon and may result from ulceration of a carcinoma of the ampulla. Icterus which subsides and is accompanied by blood in the stools suggests the presence of a papilla malignancy. Loss of weight is common and is probably attributable to the loss of appetite and gastrointestinal disturbance. Nausea and vomiting are frequent. The onset of fever may signify cholangitis. Anemia occurs in about 30 per cent of the cases (Kirschbaum and Kozoll). An enlarged gall bladder in carcinoma of the bile duct and adjacent area is more often found at autopsy and operation than by abdominal palpation. Courvoisier stated that a distended gall bladder occurs in 84 per cent of duct cancer, while in the studies of Kirschbaum and Kozoll it is nearer to 60 per cent. Biliary peritonitis has already been mentioned. Ascites occurs with peritoneal metastases. Roentgen examinations may show a widening of the duodenal curve or a duodenal obstruction in patients with pancreatic carcinoma. In rare instances neoplasms of the common bile duct papilla and pancreas may be silent and are incidental findings at autopsy.

Prognosis—The outlook for patients with malignancy of the common bile duct papilla of Vater and head of the pancreas is very grave. As a result of the deep jaundice, cholemia, cholangitis, cachexia, metastases and other complications patients unoperated upon die rapidly after the onset of symptoms.

Ninety seven of one hundred patients not subjected to surgery lived two weeks to twenty eight months and of these 80 per cent died before twelve months" (Laeher and associates for carcinoma of peripapillary area). Death occurs in from two to ten months after the onset of progressive jaundice in patients with carcinoma of the pancreas (Schnedoff and Orr).

Palliative operations aim at relieving the jaundice and pruritus but carry a high operative mortality and stave off death for a short time.

Despite the morbidity and operative mortality radical extirpation of the malignant tumor offers the only hope for cure. In the series of 124 cases of ampullary tumors reported by Hunt in 1941 93 patients were treated by trans duodenal excision. 5 patients were treated by retroduodenal removal. 11 patients were treated by resection of the duodenum with end to end anastomosis of the intestine and implantation of the ducts and 15 patients were treated by some form of resection of the duodenum and pancreas. In this group of patients about 14 per cent of those surviving operation lived from three to twenty two years after operation. Pickrell and Blalock's report of segmental resection of choledochal carcinoma disclosed that of 14 patients who survived operation and were followed postoperatively at least 4 lived for more than eighteen months. Garlock's patient lived for five years after operation but finally succumbed to metastases. As yet it is difficult to evaluate the late results and prognosis in

patients who were subjected to duodenopancreatectomy for carcinoma of the papilla or head of the pancreas. However, several patients have lived for more than two years.

The immediate operative mortality may be best summarized as shown in Table I.

TABLE I

	PER CENT
Pickrell and Blalock for suprapapillary tumors	93
Hunt for ampullary lesions	
1898 to 1925 (58 cases, series of Cohen and Colp)	41.3
1925 to 1941 (66 cases)	21.2
Whipple for duodenopancreatectomy, 41 cases (two stage operation)	29.2
Whipple for duodenopancreatectomy, 23 cases (one-stage operation)	34

The prognosis after operation is largely dependent upon recurrence of the carcinoma with metastases and the occurrence of cholangitis. The latter complication is of serious moment and has not as yet been overcome. All patients who are subjected to resection of a choledochal or periampullary carcinoma require some form of biliary intestinal restitution. End-to-end suture of the common bile duct frequently leads to stricture formation, biliary stagnation, and infection. The use of splinting tubes for the anastomosis, whether made of rubber or vitallium, may result in late incrustation of the tube and bile blockade (Bettman and Tannenbaum, Colp). The incidence of cholangitis is greater in cases where the common or hepatic ducts are reimplanted into the gastrointestinal tract. This obviously removes the normal sphincter mechanism at the papilla of Vater. Such reimplantations are an absolute necessity in duodenopancreatectomy. Bracken and David mentioned the following statements relative to anastomosis of the bile ducts to the gastrointestinal tract:

Gage. In 40 dogs subjected to choledochoduodenostomy the liver showed histologically small abscesses and necrosis.

Sandblom, Bergh and Ivv. The site of anastomosis does not affect the problem of ascending liver infection.

Bernhard. After anastomosis of the gall bladder to the gastrointestinal tract barium regurgitates into the liver.

Wilde Gans. Observed numerous cases of barium in the liver after choledochoduodenostomy.

Lahey. The majority of cases with rubber tubes in the new anastomosis develop chills, fever and jaundice.

Judd. In 47 cases of hepaticoduodenostomy, contracture of the anastomosis developed in 7 cases.

Ladd and Gross. Nine patients were well for from five to sixteen years after operations for stricture and atresia of the biliary tract.

Eliot. In 1936 collected 56 cases of hepaticoduodenostomy and found 11 patients well after ten to twenty years. Cholangitis was common.

Walters. In 1939 reported a series of 80 cases operated upon for benign stricture of the biliary ducts with good results in 68 per cent.

It has been stated that a large stoma in the new anastomosis leads to regurgitation into the biliary tree while a small stoma has a tendency to stenose. In an effort to minimize the incidence of cholangitis various suggestions have been made for biliary intestinal anastomosis after duodenopancreatectomy. Whipple advised against the use of the gall bladder for the anastomosis and considered the stomach an inadvisable site because of the strong muscular wall.

Trimble implanted the stump of the choledochus obliquely into the jejunum through a stab incision in the bowel. The method of Cole and his co-workers of making a valvelike arrangement in the blind loop of the λ to which the common duct is anastomosed has already been mentioned. Bracken and David advocated the use of a cutting suture to unite the bile duct and bowel. It appears logical that a Roux type of bile duct to intestinal anastomosis may minimize the incidence of cholangitis and it would be wise to perform the gastro-intestinal anastomosis distal to the biliary intestinal anastomosis.

The problem of postoperative cholangitis is one that is yet to be solved.

Treatment—It is not the scope of this presentation to describe the infinite details which are involved in operations for the removal of malignant tumors involving the choledochus perianillary region or head of the pancreas. The technique has already been well described (Whipple, Hunt, Brunschwig and others). The present consensus favors a one-stage operation. It should be planned in such a manner that the procedure can be terminated within a short time for a staged operation if the condition of the patient warrants early termination of the operation. Careful preoperative preparation with fluids, plasma, whole blood and vitamin K are necessary. The anesthesia must be chosen carefully for the procedure is time consuming. Continuous spinal anesthesia is of great help. An adequate supply of whole blood during the operation is advisable to combat shock and blood loss. A complementary jejunostomy for feeding is suggested for use in some cases as an aid in the early convalescent period. Biliary and pancreatic leaks are frequent and troublesome so that adequate drainage is necessary. The prophylactic use of penicillin may be of value in the prevention of infection.

CONCLUSIONS

1. Two cases of segmental resection of the common bile duct for cancer were presented. In one case a rare anomaly of the biliary ducts necessitated a separate anastomosis of each hepatic duct with the duodenum. Both patients survived operation.
2. Two cases were presented of one-stage duodenopancreatectomy. In one patient the neoplasm involved the lower end of the common bile duct while in the other the tumor was situated in the head of the pancreas.
3. A discussion of the historical features, incidence and pathology of choledochal neoplasms was presented.
4. The problem of cholangitis which follows operations for stricture of the common bile duct or biliary intestinal anastomosis is yet to be mastered.

patients who were subjected to duodenopancreatectomy for carcinoma of the papilla or head of the pancreas. However, several patients have lived for more than two years.

The immediate operative mortality may be best summarized as shown in Table I.

TABLE I

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The Miller Abbott tube is especially useful in that group of cases in which circulatory changes (strangulation) in the bowel require immediate surgical intervention. In this category postoperative intubation is a valuable adjunct in preventing further distention and in contributing to the restoration of normal intestinal tone and function.

Postoperative intubation is also of value in relieving tension on suture lines following elective intestinal resections and anastomoses.

Least this classification be considered as indicating the desirability of intestinal suction in all cases of obstruction the contraindications should also be emphasized. When there is a reasonable possibility of vascular strangulation of the bowel intubation should not be attempted except as a preparation for immediate operation. The danger is that although decompression offers no beneficial relief in vascular obstruction it may in fact mask the symptoms to such an extent as to minimize the urgency of operation which is the essential therapy for intestinal strangulation. The decision for immediate surgery depends upon all the available clinical facts at hand and if strangulation cannot be ruled out surgery is indicated. Willson and others have shown that intestinal suction should not be resorted to in cases of obstruction of the large bowel which show great distention of the colon and little or no evidence of small bowel involvement. In these cases of so called closed loop obstruction of the colon the ileocecal valve is still competent and does not permit the pressure within the large bowel to be relieved by regurgitation into the ileum. Accordingly intestinal intubation is not the treatment of choice because the relief of pressure in the large bowel may be unwisely delayed.

Complications.—Although its advantages are unquestioned intestinal intubation if used unwisely may lead to serious and even fatal complications. In the employment of an indwelling tube for the relief of intestinal distention it is of great importance that the surgeon remember that this therapeutic method like many others produces a combination of desirable and undesirable results and in any particular case the indications for its use must be such that the advantages far outweigh the disadvantages. It is therefore worth while to point out some of the undesirable effects and complications which may occur during continuous suction drainage of the intestinal tract with the Miller Abbott tube.

Murphy,⁵ Brooks,⁶ Romano,⁷ Wangensteen,⁸ and Taylor⁹ have discussed in considerable detail the physiologic changes and the fluid electrolyte and mineral imbalances which occur as a result of the continuous withdrawal of intestinal contents by means of suction drainage. They have also indicated the importance of and the methods of adequate replacement therapy so that these factors will not be reviewed here.

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The problem of how long intubation may be used with impunity arises. Although in the average case suction intubation usually accomplishes its purpose in one to three days occasionally distention may persist to such a degree

PERFORATION OF THE SMALL INTESTINE BY THE MILLER ABBOTT TUBE

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ACCIDENTS and complications have been reported with the use of the Miller-Abbott tube. However, in reviewing the literature, we have failed to note a single case of perforation of the small bowel during intestinal intubation. It is the purpose of this communication to point out some of the dangers involved in the procedure of intestinal decompression by intubation and to present a case report of small bowel perforation by the Miller-Abbott tube.

Before considering the dangers associated with intestinal intubation in bowel obstruction, it is logical to review the indications and contraindications of this procedure.

Twelve years have elapsed since Miller and Abbott¹ first advocated the use of the double lumen balloon tipped tube for the control of distention in the obstructed intestine, eight years of clinical experience following its first reported application by Abbott and Johnston² in 1938 have demonstrated definite indications for, as well as contraindications to, its use.

Wangensteen³ and Dearing⁴ have classified the intestinal obstructions into three major clinical groups and have indicated the role of intubation in each category.

Obstructions Suitable to Treatment by Intubation Alone—The first group includes cases of paralytic or adynamic ileus where there is considerable distention of the intestine without mechanical factors. This may be produced reflexly by trauma, especially to the spine, by ureteral colic, etc., or the ileus may result from an intraperitoneal inflammatory process, for example, primary hemotogenous peritonitis. In such cases intubation often lessens distention so that surgical intervention for the relief of distention per se is unnecessary.

Obstructions Where Intubation Is a Preoperative Adjunct—The second group includes the various types of mechanical obstructions in their early stages. The obstruction may be the result of extraluminal, intramural or intraluminal causes. As a rule decompression of the distended intestines under these circumstances, is a preliminary procedure designed to facilitate subsequent surgical intervention.

Obstruction Where Intubation Is Utilized Postoperatively—Most cases of immediate postoperative abdominal distention are relieved by suction via a single lumen (Levine) tube. However there are occasional cases in which the distention persists because it results from the presence of early postoperative fibrinous adhesions. It is felt by many surgeons that the absorption of these adhesions is enhanced by the use of the Miller-Abbott tube.

necrosis Death was attributed to peritonitis following perforation of the anterior stomach wall, plus massive atelectasis of the lungs

Although a review of the literature failed to reveal any reports of a similar accident, it has been stated by Wangenstein⁴ that upon inquiry of various pathologists in Minneapolis and St. Paul he learned that an occasional small erosion of the gastric mucosa had been observed following the use of various gastrointestinal tubes

Mahon also cited Glassman¹⁵ and Wolf,¹⁶ who have reported series of cases of rupture of the stomach. "In some of these the accident occurred during lavage for an obstructive pyloric lesion in others during intubation for removal of fluid and gas from an overfilled stomach." The outcome in most of these was usually fatal.

Finally, Lemmon and Paschal¹⁷ described a case in which the patient also died from rupture of the stomach. The fatality in that case was attributed to a delay in operating while awaiting improvement by intubation and parenteral fluid administration.

The following case report is presented to illustrate another type of complication resulting from the use of the Miller Abbott tube, which, to our knowledge has not been previously reported.

CASE REPORT

P. C., a 40-year-old married woman was first admitted to the Jewish Hospital of Brooklyn on March 25, 1944, complaining of a mass in the right abdomen associated with intermittent pain for five months. The mass was palpable by the patient in the right hypochondrium and the pain, which gradually increased in severity was always referred to the right upper quadrant. There was no history of weight loss, melena, or change in bowel habits. A work-up, which included intravenous urography, a gastrointestinal series, and a barium enema, revealed the presence of a carcinoma of the colon in the region of the hepatic flexure. The patient also exhibited evidence of a moderate secondary anemia. Five days of preoperative preparation were given. During this period, the hemoglobin was improved with two blood transfusions; a positive nitrogen balance was obtained by the administration of daily parenteral amino acid preparations, and the liver was fortified with intravenous glucose and vitamins. In addition, a reduction in the bacterial (coliform) flora of the intestinal tract was accomplished by giving the patient sulfasuxidine (succinyl sulfathiazole) orally.

The patient underwent a laparotomy on April 18, 1944. As suspected, an annular tumor of the hepatic flexure was encountered. A right hemicolectomy was performed with immediate aseptic anastomosis over Furness clamps (end to side ileotransverse colostomy). The microscopic pathologic diagnosis was adenocarcinoma. The postoperative course was uneventful, and the patient was discharged on May 8, 1944, the twentieth postoperative day. She returned to work in July 1944, and remained free from symptoms. In October, 1945, a check-up barium enema revealed no unusual findings. The anastomosis was patent and functioned properly.

On April 1, 1946, two years after the colectomy, the patient experienced a sudden onset of sharp epigastric pain which radiated along both costal margins. It was severe enough to require frequent injections of morphine during the next four days. Associated with the pain there was nausea, vomiting, and gradually increasing abdominal distention. The patient did not have a bowel movement following the onset of the pain, but she was able to pass small quantities of flatus per rectum.

She was readmitted to the Jewish Hospital of Brooklyn on April 5, 1946, on the fourth day of the illness. The patient appeared markedly dehydrated. The abdomen was dis-

and for so long as to require continuous drainage over a period of many days or even weeks. Herein lies another danger of the procedure. It must be remembered that the tube may incite a reaction anywhere along its course in the gastrointestinal tract. Several illustrations of involvement of the nasopharynx, larynx, esophagus, and stomach have been reported in the literature. Vinson¹¹ cited three cases of esophageal stricture resulting from prolonged intubation following abdominal operations. All three patients recovered although the ensuing strictures necessitated repeated dilations in each case. Isbauer and Molt¹² have discussed the possibility of permanent injury to the larynx. They reported ten cases of laryngeal edema produced by indwelling tubes in eight of which tracheotomy was necessary. In their group of cases the tube was retained in place for periods varying from six to twenty days. They observed that the symptoms were gradual in onset usually occurring after the tube had been permanently removed and increasing until tracheotomy became imperative. Two cases came to autopsy: one showed deep ulceration of the upper end of the esophagus, the other exhibited shallow linear ulcers in the upper esophagus associated with marked laryngeal inflammation. These authors stressed the fact that laryngeal edema, although severe may escape notice in an extremely ill patient. In one of their cases the patient while unconscious was fed through a Levine tube for five days. The obstruction resulting from the laryngeal edema did not become apparent until consciousness returned. Kaufman and associates¹³ reported a case of laryngeal edema in a patient who was receiving Miller Abbott intubation. Although the edema was relieved by tracheotomy the patient died three days later. At autopsy the larynx was edematous and the mucosa of the trachea was intensely congested and covered by a fibrinopurulent exudate. Death was attributed to toxemia inasmuch as the patient was also suffering from several organic diseases.

Two cases of injury to the arytenoid cartilages¹⁴ following prolonged intubation were reported by Wangenstein in 1939. In one of these cases the patient required a tracheotomy and was left with some permanent limitation of motion in one of the vocal cords. In the other case the edema subsided after drainage of an abscess.

Morrison¹⁵ in his textbook of otorhinolaryngology also referred to cases of laryngeal injury from the wearing of a duodenal tube. He stated that cricoid chondritis may occur when a rubber feeding tube has been retained in the esophagus for long periods.¹⁶

Mahon¹⁷ in a paper which reviews some of the pertinent literature reported a case of multiple perforations of the stomach with peritonitis following Levine tube drainage. This patient required Levine tube suction drainage for a period of one week postoperatively following a partial small bowel resection for acute intestinal obstruction. Two days after removal of the tube the patient developed severe dyspnea necessitating an emergency tracheotomy. This afforded transient relief but the patient died ten hours later. Autopsy revealed four areas of necrosis on the anterior wall of the stomach just above the greater curvature. Perforations had occurred through two of these presumably by pressure.

tended and tympanic. A scout film of the abdomen revealed diffuse distention of both large and small bowel loops (Fig. 1). There was no clinical evidence of circulatory embarrassment of any bowel segments. The patient's nitrogen find and electrolyte balance was restored with continuous parenteral administration of glucose, saline, and protein solutions. A Miller Abbott tube was introduced on April 7, 1946 and attached to a Wangenstein continuous suction apparatus. The tube passed the pylorus and entered the duodenum without any undue delay. It then progressed down through the jejunum to the ileum. Considerable amounts of small intestinal fluid contents were removed by the suction drainage and as the tube progressed the abdominal distention diminished (see Figs. 2 and 3). On April 11, 1946 a scout film (Fig. 4) revealed the tip of the tube in the right upper quadrant. At no time did the tube progress beyond this point. Repeated attempts to facilitate further passage were made by withdrawing the tube for a distance of eighteen inches and permitting it to progress again. After each partial withdrawal the abdominal distention and pain

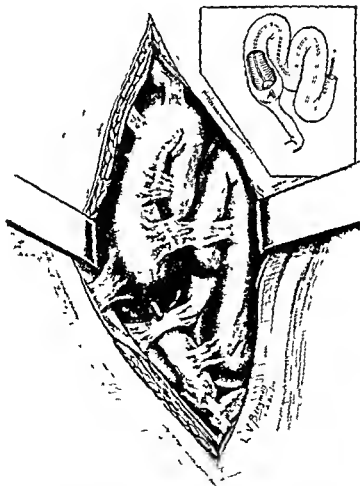


Fig. 4—Illustrating the perforation which the balloon inflated tube had perforated through the wall of the ileum proximal to the point of obstruction.



Fig 1



Fig 2



Fig 3

Fig 1—A cut off of the ablo n revealing diffuse distention of host tissue n l e H l o w 1 1 1 4
 Fig 2—Distortion in the leg o f i t e s t h a t d i t e n t i o n r e s u l t i n g f r o m M i r A b u t t h o l T a t
 Fig 3—Same as Fig 1 t h e t h o s e n o w l o c a t e d i n t h e r i g h t h e r e q u i r e

tended and tympanic. A scout film of the abdomen revealed diffuse distention of both large and small bowel loops (Fig 1). There was no clinical evidence of circulatory embarrassment of any bowel segments. The patient's nitrogen fluid and electrolyte balance was restored with continuous parenteral administration of glucose, saline, and protein solution. A Miller Abbott tube was introduced on April 6, 1946 and attached to a Wangensteen continuous suction apparatus. The tube passed the pylorus and entered the duodenum without any unusual delay. It then progressed down through the jejunum to the ileum. Considerable amounts of small intestinal fluid contents were removed by the suction drainage, and as the tube progressed the abdominal distention diminished (see Figs 2 and 3). On April 11, 1946 a scout film (Fig 3) revealed the tip of the tube in the right upper quadrant. At no time did the tube progress beyond this point. Repeated attempts to facilitate further passage were made by withdrawing the tube for a distance of eighteen inches and permitting it to progress again. After each partial withdrawal the abdominal distention and pain

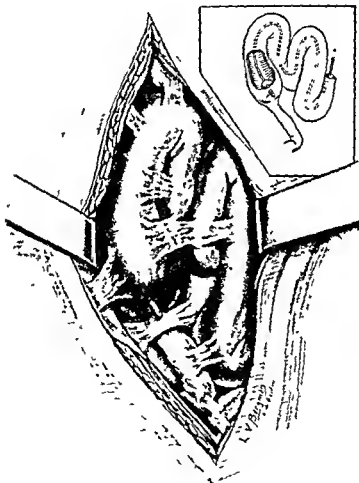


Fig 4.—Illustrating the manner in which the balloon inflated tube had perforated through the wall of the ileum proximal to the point of obstruction.

recurred, but as the tube progressed again, the symptoms and signs of obstruction subsided. During this period a moderate amount of flatus was expelled per rectum as a result of colonic irrigations.

On April 12, the distention and pain had diminished so considerably that the Miller Abbott tube was clamped and fluids were permitted by mouth. One hour later the patient vomited, and therefore the suction drainage was quickly resumed. During the next few days the amount of drainage via the Wangenstein apparatus diminished rapidly. For one day prior to operation there was no drainage at all. It should be stated that during this period, when the patient's condition was gradually becoming worse, operation was advised and even strongly urged for a period of one week. However, because the senior author, who had previously performed the colectomy, was away on vacation, the patient did not consent to operation until his return on April 17, 1946.

On April 18, 1946, twelve days after the Miller Abbott tube had been introduced as exploratory laparotomy was performed. On opening the peritoneal cavity a moderate amount of serous fluid was encountered. Several loops of ileum were adherent to each other and to the anterior parietal peritoneum in the region of the first operative scar, one of the adhesive bands had constricted the bowel lumen to such a narrow diameter that it did not permit the Miller Abbott tube with its inflated balloon to pass beyond this point. Immediately proximal to this point of obstruction there was a perforation in the wall of the ileum through which the metal tip of the tube protruded into the peritoneal cavity. Apparently the inflated balloon had acted as a check valve to prevent further progression of the tube through the wall of the ileum into the peritoneal cavity (Fig. 4). The bowel wall immediately adjacent to the perforation was neutely inflamed and covered by a fibrinoplastic exudate. There was no evidence of strangulation of bowel, or of gross leakage of ileal contents into the peritoneal cavity, inasmuch as the various loops of small bowel had completely walled off the perforation from the general peritoneal cavity. Furthermore, there was no gross evidence of recurrent carcinoma at the site of the previous bowel resection or in the form of metastases elsewhere.

The metal tip of the tube was withdrawn into the lumen and the perforation in the bowel wall closed with two layers of silk sutures. Lysis of the adhesive bands was effected in such a manner as to eliminate the kinks in the bowel loops. Complete intestinal continuity without obstruction was thus restored. The Miller Abbott tube was left in situ. The wound was closed in layers, using steel alloy wire sutures.

The postoperative course was completely uneventful. The Miller Abbott tube was removed on the first postoperative day and the patient was given fluids orally. Signs and symptoms of obstruction did not recur. The patient had a spontaneous bowel movement on the fourth day. She was discharged symptom free on the tenth postoperative day, and at the time of this report was enjoying good health.

This case is a dramatic example of the complications which may occur from the overprolonged use of the Miller Abbott tube in the treatment of intestinal obstruction.

COMMENT

Gastrointestinal intubation may be considered one of the most significant contributions to surgery in the present century. In our experience, as well as in that of others, it has been instrumental in the saving of many lives. The procedure, however, has certain limitations. Irreparable injury and even death may

whic
during intubation. Although errors in its use are comparatively few yet they are of sufficient seriousness to cause us to give thought to its potentialities for

port of a case
small intestine

harm Urburu,^{18 19} in two admirable articles, has reviewed the difficulties in the technique of passing the tube, and has suggested various methods of correcting these defects in order to obtain the best therapeutic result in each case. Harris²⁰ has further contributed to the progress of intestinal intubation by describing the clinical use of a single lumen mercury weighted tube which has certain excellent technical advantages over the time honored Miller Abbott tube.

Aside from the difficulties in the technique and proper maintenance of suction, we should like to stress the importance of early recognition of the signs and symptoms of complications which arise from the very presence of the tube itself in the gastrointestinal tract. Prolonged intubation should be accompanied by frequent x rays or fluoroscopy to check the position of the tube. The surgeon should not be lulled into a false sense of security by the apparent improvement in the patient's general condition. Intubation with the Miller Abbott tube to be effective must show rapid and progressive improvement in the signs of intestinal obstruction. Improvement to be considered significant must continue even after the suction drainage has been discontinued and the tube has been clamped off. Any deviation from this simple premise invites the danger of fatality. Although the measure of usefulness of the Miller Abbott tube far outweighs the total number of collected cases which illustrate its harmful effects, it is to be hoped that eventually the latter will be completely eliminated. Careful clinical attention to details of procedure will promote this fulfillment.

SUMMARY

1 A brief résumé of intestinal intubation has been presented, together with a discussion of the indications and contraindications for the use of the Miller Abbott tube.

2 Complications resulting from the use of the Miller Abbott tube have been mentioned and illustrated by examples from the current literature.

3 A case is presented which illustrates one further type of complication which has not been previously reported.

4 The dangers involved in the indiscriminate or overprolonged use of this valuable adjunct to abdominal surgery have been stressed.

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THE SURGICAL MANAGEMENT OF GASTROJEJUNOCOLIC FISTULAS

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INTRODUCTION

BRAUN, in 1899 reported the first gastrojejunal ("marginal") ulcer and in 1903 Czerny reported the first gastrojejunocolic fistula. Each of these conditions occurred as a complication following posterior gastrojejunostomy performed for duodenal ulcer. Since 1903 an increasing number of cases of gastrojejunocolic fistulas have been reported and number at the present approximately three hundred. This figure includes only those cases occurring as a complication following operation for gastric or duodenal ulcer.

The seriousness of a gastrojejunocolic fistula was soon demonstrated by the prohibitive mortality which occurred following attempts at correction (Table V). This high mortality rate served as a stimulus which resulted in the development of many and varied methods of surgical management, all aimed at a lowering of the operative death rate.

Unfortunately the number of patients with gastrojejunocolic fistula treated by any one method is too small to be of statistical value. Therefore, in evaluating any particular method of surgical management, the important consideration is the logic which forms the basis for treatment. With this in mind we reviewed the development of the surgical treatment of gastrojejunocolic fistula and considered the multi stage method with the use of a preliminary colostomy as described by Pfeiffer the most logical from the surgical standpoint.

In the five year period from 1939 to 1944 we treated surgically six patients with gastrojejunocolic fistula. A preliminary colostomy was employed with satisfactory results in a consecutive series of five of the six cases. Although this series is small it is the largest single series reported with this type of treatment. These five cases plus a case of Mathewson's,¹⁷ when added to the collective series reported by Pfeiffer¹⁸ (1941), total twenty one. All of these patients were treated by preliminary colostomy with one death (4.8 per cent). There is no doubt that more have been treated in this manner but they were isolated cases and not reported.

It is our opinion that the value of performing a preliminary colostomy in the treatment of gastrojejunocolic fistula has not been generally recognized or sufficiently stressed. Since it is not the lot of any one person to treat many patients with gastrojejunocolic fistula, we wish to report our experience in the surgical management of six cases, stressing in particular the merits of performing a preliminary colostomy.

Information which may be of future statistical value is presented in Tables I to V.

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CLINICAL DISCUSSION

The six patients treated were all men. The average age was 43.5 years, the youngest was 29 and the oldest 53. The fistula in each case occurred as a complication of a posterior gastrojejunostomy done for duodenal ulcer. There was a history of a "marginal" ulcer in two cases and a questionable history in one case. The outstanding symptoms (Table I) were diarrhea and weight loss. These symptoms were present in all patients. In one patient between thirty and forty bowel movements occurred during a twelve hour daytime period. The greatest weight loss was sixty pounds and the average weight loss was forty pounds. Abdominal pain and a sense of weakness were the symptoms next in frequency. A slight to moderate amount of anemia was present in four cases. Undigested food particles were noted in the stools in three cases. Stercoraceous vomiting and eructations with a fecal odor were present in three cases. A clinical deficiency state was present in three cases. Impairment of appetite was noted in only one patient.

TABLE I. SYMPTOMS IN ORDER OF FREQUENCY OF OCCURRENCE

- 1 (a) Diarrhea
(b) Weight loss
- 2 (a) Abdominal pain
(b) Weakness
(c) Anemia
- 3 (a) Stercoraceous vomiting
(b) Eructations with a fecal odor
(c) Undigested food particles in stools
- 4 Malnutrition
- 5 Impairment of appetite

The shortest history of ulcer pain prior to operation (posterior gastrojejunostomy) was three years and the longest fifteen years with an average of seven years. Relief of ulcer symptoms following operation occurred in all cases and varied from six months to nineteen years with an average period of 6.6 years (Table II). Following a barium enema roentgenographic demonstration of the fistula was obtained in each case. However following a barium meal the fistula was visualized in only three of the six cases.

The average duration of symptoms referable to a gastrojejunocolic fistula was fourteen months. The shortest period was five weeks and the longest six

TABLE II. SUMMARY OF SIX CASES IN WHICH POSTERIOR GASTROJEJUNOSTOMIES WERE DONE

CASE NUM REFS	AGE	SEX	DURA TION OF ULCER SYMPTOMS PRIOR TO OPERA TION (YR)	RELIEF OF SYMPTOMS FOLLOWING GASTROJE JUNOSTOMY	DEVELOPMENT OF A MARGINAL ULCER FOLLOWING GASTRO JEJUNOSTOMY	DEVELOPMENT OF A GASTRO- JEJUNOCOLIC FISTULA FOLLOWING GASTRO- JEJUNOSTOMY
1	46	Male	9	16 mo	10 mo	16 1/2 mo.
2	53	Male	1 1/2	4 yr	Negative history	4 yr
3	37	Male	3	10 mo	10 mo	22 mo
4	35	Male	3	6 mo	6 mo	7 yr
5	52	Male	5	19 yr	Negative history	19 yr
6	45	Male	6	14 yr	Negative history	14 yr

years (Table II) In the latter case, fecal vomiting had been present for two years and diarrhea for six years There was an associated severe nutritional deficiency The patient was a chronic and complete invalid as the result of the illness

A preliminary ascending loop colostomy was done in five of the six cases Following colostomy a rapid improvement in the clinical condition of each patient occurred There were pronounced beneficial effects in reference to the diarrhea, vomiting, and weight status In three of the patients there was an immediate and complete cessation of the diarrhea following colostomy In the remaining two a moderate to marked improvement in the diarrhea occurred However, in one of the latter, loose stools per rectum persisted and contained undigested food particles This would indicate a direct passage of food from the stomach through the fistula into the colon Stercoraceous vomiting and foul eructations which were present in three cases ceased immediately A gain in weight occurred in each patient varying from a low of eight pounds to a high of twenty five pounds

From our own clinical observations we are in agreement with Pfeiffer¹⁹ (1941) in reference to the etiology of the diarrhea in cases of gastrojejunoecolic fistula This author believed that the diarrhea was secondary to the regurgitation of irritating colon contents into the stomach and jejunum This produced a hyperperistalsis in the jejunum and a rapid passage of the small intestinal contents into the colon In support of this concept is the clinical observation of immediate cessation or marked improvement in the diarrhea that occurs following a colostomy proximal to the fistula Additional support has been obtained by fluoroscopic study and roentgenograms in three ways, namely, (1) the rapid passage of barium through the small intestines into the colon (2) the comparative infrequent demonstration of the fistula by barium meal, and (3) the ease and frequency with which the fistula has been demonstrated by barium enema Observations in the operating room and dissecting room have shown frequently the presence of a valvelike mechanism of the intestinal mucosa folds about the fistula which facilitated passage of colon contents into the stomach and jejunum but not the reverse

Prior to this concept it was the prevalent opinion that the cause of the diarrhea was the direct passage of stomach contents through the fistula into the distal colon That this may still remain a factor in some cases is not denied We previously cited our experience in one case in which diarrhea and the passage of undigested food particles persisted subsequent to a proximal colostomy However this may be considered an infrequent occurrence

From the foregoing it may be stated that in a patient who develops an intractable diarrhea and has a previous history of having a gastrojejunostomy performed for ulcer, a gastrojejunoecolic fistula should be considered as a possible causative factor

TREATMENT

In the treatment of the first reported case of a gastrojejunoecolic fistula (Czerny, 1903), a resection en bloc of the stomach, jejunum, and colon was done and a gastroenterostomy successfully re established Subsequent to this

and until a comparatively recent date this one stage operation remained the treatment of choice. This operation usually consisted of a disconnection of the fistula and a simple restoration of normal gastrointestinal continuity.

In an attempt to improve the results of surgical management modifications of the one stage operation were introduced. Mason and Baker⁶ (1931) advocated a complementary exteriorization of the transverse colon at the time of resection of the fistula in an attempt to reduce the hazard of leakage at the suture line and peritonitis. Three patients were reported treated in this manner with one death. Lahey and Swinton¹² (Fig 1) treated two patients by an exclusion operation. The stomach was divided proximal to the fistula and an end to side gastrojejunostomy performed by passing the fistula.

GASTRIC RESECTION
AND ANTECOLIC
GASTROJEJUNOSTOMY
STAGE II

ILEOCOLOSTOMY
STAGE I

LEUM

OPERATION SUGGESTED

LAHEY
1935

JEJUNUM

FISTULA

OPERATION PERFORMED

LAHEY
1935

FIG 1

Allen¹ favored the use of an en bloc resection of the fistula and an aseptic anastomosis to avoid the lethal complication of peritonitis. Collier⁸ advocated a period of adequate preoperative preparation of the patient and reported a reduction in the mortality rate from 40 to 12 per cent under this regime. In support of this Gray and Sharpe² following a period of intensive preoperative preparation reported a reduction in the mortality rate from 61.5 to 27.7 per cent.

However in general there was increasing dissatisfaction with the one stage operation because of the associated high incidence of postoperative peritonitis. It has been stated (Lindlay) that peritonitis has accounted for 60 per cent of the deaths following operations for gastrojejuno-colic fistula.

To avoid the serious complication of peritonitis various multi stage operations were developed. Lindlay⁹ (Fig 2) suggested the exteriorization of the

transverse colon (von Mikulicz) with the attached jejunal segment that contained the fistula, simple closure of the gastric stomach and an end to end anastomosis of the jejunum. Serimger²² (Fig 3) advocated the use of a gastric cuff from that portion of the stomach wall to which the jejunum was attached

FINDLAY

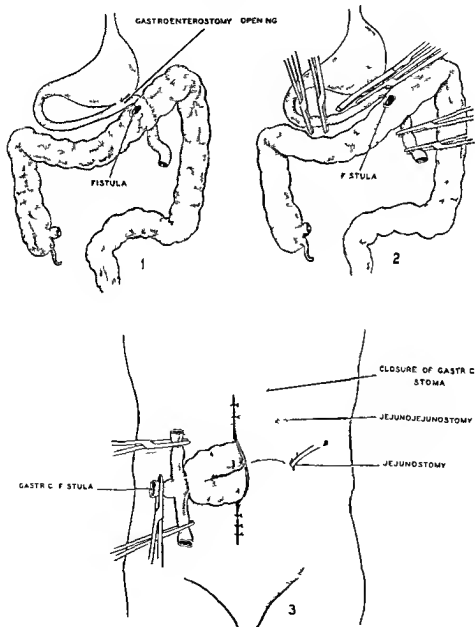
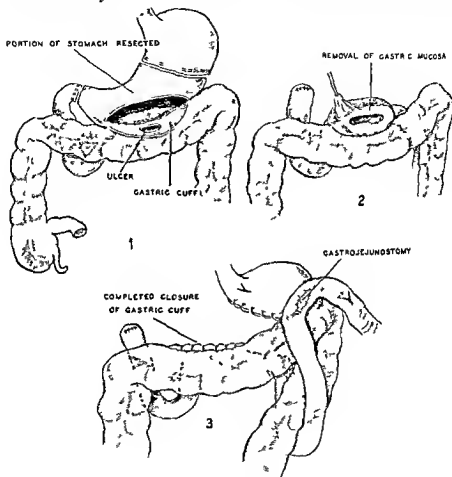


Fig 2.

The mucosa of the gastric cuff was then removed and the two opposing surfaces sutured together, muscularis to muscularis. Subsequent to this a subtotal gastric resection was done. This operation was based on the principle that if a jejunal ulcer was shut away from the gastric contents it would heal. Second, if exclusion of the jejunal ulcer could be accomplished without encroaching on the ulcer, a resection of the jejunum and transverse colon would not be necessary.



SCRIMGER

FIG. 2

Dr. Scrimger (Fig. 2) presents a very logical multi stage operation as done as the first stage. Three to four weeks later a gastrojejunostomy was done. This consisted of a disconnection of the fistula and a simple restoration of gastrointestinal continuity or a subtotal gastric resection (preferred). The closure of the colostomy three to four weeks later, completed the operation.

Independent of Pfeiffer Baker¹ (1940) advised a preliminary defunctioning ileostomy. One week subsequently the fistula was disconnected and a subtotal gastric resection was done.

Recently Marshall¹⁵ (Fig 5) presented a modification of the two stage procedure suggested by Lahey and Swinton¹³ (Fig 1). In the first stage a side to side ileocolostomy was done between the terminal ileum and the descending colon with a terminal ileal exclusion. The second stage two to three months later consisted of a block excision of the jejunum and involved colon jejunocolostomy subtotal gastric resection and removal of the terminal ileum cecum ascending and transverse colon to a point distal to the fistula. He reported fourteen patients treated in this manner with one death (7.1 per cent). Closure of the colonic fistula occurred in two cases following the first stage ileocolostomy.

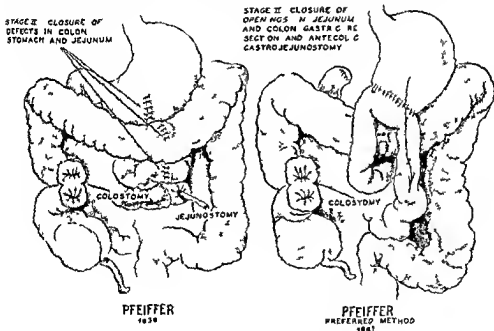
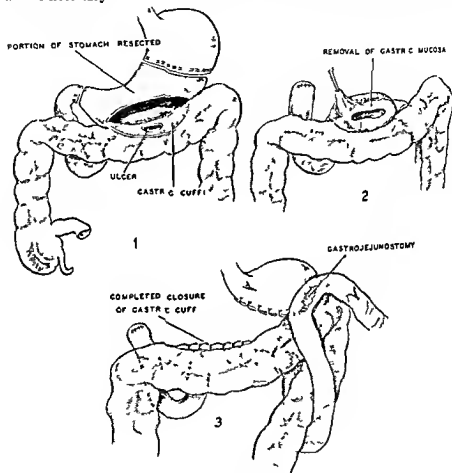


FIG 4

In the evaluation of any particular method of treatment there are many factors to be considered. These factors are the age and general condition of the patient, the size of the fistula, the severity of the symptoms, and the response to preoperative treatment. Each case must be rigidly individualized. Following a review of the early methods of surgical management, the excessive mortality appeared to be related to four main factors: (1) the severe malnourishment and poor general condition of the patient; (2) the lack of an adequate period of preoperative preparation of the patient; (3) the technical difficulties encountered at operation; (4) the high incidence of peritonitis secondary to the leakage of colon contents.

The mucosa of the gastric cuff was then removed and the two opposing surfaces sutured together, muscularis to muscularis. Subsequent to this a subtotal gastric resection was done. This operation was based on the principle that if a jejunal ulcer was shut away from the gastric contents it would heal second if exclusion of the jejunal ulcer could be accomplished without encroaching on the ulcer, a resection of the jejunum and transverse colon would not be necessary.



SCRINGER

FIG. 3

Pfeiffer and Kent¹⁸ (Fig. 4) presented a very logical multi stage operation. A preliminary ascending loop colostomy was done as the first stage. Three to four months later the definitive operation was done. This consisted of a disconnection of the fistula and a simple restoration of gastrointestinal continuity or a subtotal gastric resection (preferred). The closure of the colostomy three to four weeks later completed the operation.

Furthermore, the marked improvement in the general condition of the patient, the subsidence of the local inflammatory reaction about the fistula and the lack of danger of peritoneal contamination with colon contents permit the surgeon to do a radical operation with a minimal risk. Moreover, this method is applicable to those patients who are in poor general condition and have large fistulas.

The use of this method has been justified following a study of the therapeutic results that have been obtained. Mathewson¹⁷ (1941) reported three patients treated by preliminary colostomy with excellent results. A transverse colostomy was preferred to an ascending colostomy. In each case a subtotal gastric resection was done at the second stage operation. In one of the cases an intraperitoneal leakage at the site of repair of the fistulous opening in the colon was demonstrated by roentgenogram (barium enema). Recovery was without incident because of the protection afforded by the proximal colostomy. Colp¹ reported a spontaneous obliteration of the fistula proved both by roentgenogram (barium enema) and at subsequent operation. Pfeiffer¹⁸ (1941) reported a collective series of fifteen cases, the patients treated by preliminary colostomy with one death (6.6 per cent), the lowest mortality heretofore published. This series included two of the three cases reported by Mathewson¹⁷ and the case recorded by Colp.¹

In contrast the two stage procedure reported by Marshall¹⁹ has the main objection of performing an intraperitoneal anastomosis involving the colon as the first stage. Regardless of how aseptically an anastomosis may be done the danger of leakage and peritonitis always exists. A second objection is the removal of such a large portion of the colon. Although this may not be considered formidable technically we believe it to be too extensive an operation for the condition treated.

Objections have been raised to the use of a preliminary colostomy: (1) it subjects the patient to a subsequent wound infection; (2) it interferes with mobilization of the bowel during the second stage; (3) it necessitates an additional operation for closure of the fistula; (4) it prolongs hospitalization. The first two objections have not proved of any practical significance. The last two are minor considerations when compared to the seriousness of the illness for which the colostomy was done.

There has been a difference of surgical opinion as to the ideal definitive operation in the treatment of gastrojejunocolic fistula. Some prefer closure of the fistula and restoration of normal gastrointestinal continuity; others believe that gastric resection rather than simple restoration should be done.

The use of the first method is dependent upon the presence of a patent pylorus. This method has been used more frequently than any other, mainly because of the belief that it afforded the minimal surgical risk. Satisfactory results have been obtained in those cases in which the patient was in good general condition and the fistula small. However, the danger of a complicating peritonitis and the high incidence of recurrence of ulcer symptoms following operation are important objections to this method. Pfeiffer reported a

Control of one or more of these factors has been attempted in the development of improved methods of treatment. The importance of an adequate period of preoperative preparation has been mentioned.¹¹ However an unduly high mortality will continue to exist unless the complicating factor of peritonitis is controlled. The chief sources of peritoneal contamination are the extensive inflammatory reaction of the tissues about the fistula and the ever present danger of leakage of colon contents at operation. It is therefore logical to assume that any method of surgical management which does not include the control of peritoneal contamination is not wholly a legitimate

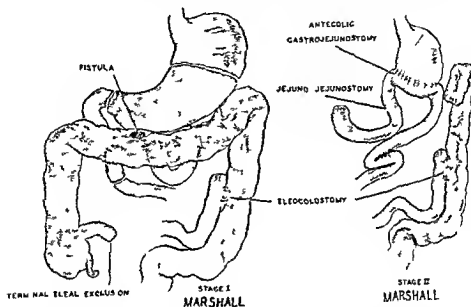


FIG. 5

After reviewing the various prescribed methods of treatment of gastrojejunocolic fistula we prefer the method of Pfeiffer.⁹ The proclaimed advantages of a preliminary ascending loop colostomy are namely (1) cessation of diarrhea with a return of the patient to excellent physical status and hence reduction of the general risks of surgical intervention (2) subsidence of the inflammatory reaction of adjacent tissues and the jejunal ulceration thus reducing the risk of inflammatory complications in the surgical correction of the fistula (3) freedom of contamination at operation and the later protection of suture lines in the repaired colon abolishing the danger of leakage. To these advantages may be added the technical simplicity of the operation. This is an important consideration because the patient is generally a poor surgical risk.

From a study of the alleged advantages of a preliminary colostomy we learn that it controls not one but all those factors which have been responsible for the prohibitive mortality in the treatment of gastrojejunocolic fistula.

FOLLOW UP STUDY

A complete follow up was obtained in all cases. The shortest follow up period was three years and four months the longest eight years and six months.

In the follow up study the cases were classified into two groups according to the type of definitive operation performed (Table III). Each group comprises three cases.

TABLE III DEFINITIVE OPERATIONS PERFORMED*

GROUP	OPERATION	NUMBER OF CASES
I	A Disconnection of the fistulous communication and gastroenteric anastomosis, simple closure of the openings in the stomach and colon resection of the jejunum and end to end anastomosis	3
	B Disconnection of the fistulous communication and gastroenteric anastomosis, simple closure of the openings in the stomach colon and jejunum	2
		1
II	Disconnection of the fistulous communication and	3

of Group I.

TABLE IV POSTOPERATIVE COMPLICATIONS

*Secondary to closure of colostomy

†Secondary to sulfadiazine therapy

TABLE V MORTALITY RATES FOLLOWING OPERATION FOR GASTROJEJUNOCOLIC FISTULAS

AUTHOR	YEAR	NUMBER OF CASES	NUMBER OF DEATHS	MORTALITY PER CENT
Lacey	1921	67	17	27.0
Verbrugge	1925	20	5	25.0
Lahey and Swinton	1935	8	5	63.0
Winterer	1938	11	5	45.4
Walters and Clagett	1938	50	16	32.0
Gray and Sharpe	1941	49	18	36.7
Isfahani*	1941	15	1	6.6
Thomas†	1940	5	1	20.0
Matheson†	1941	3	0	0.0
Atwater et al	1943	41	11	27.0
Ransom†	1945	14	2	14.3
Marshall	1945	14	1	7.1
Barber and Midden†	1946	6	0	0.0

* if the three cases are included in the collective mortality rate of Pfeffer (1941). Each case

† reported by Pife (1935)

recurrence rate of 25 per cent Lahey 40 per cent In our own experience with three patients treated in this manner a recurrence of ulcer symptoms occurred in each one

In reference to gastric resection it is the opinion of many that it is too formidable an operation to do following the ablation of the fistula They believe a resection should be done at a subsequent stage and then only if there has been a reactivation of the ulcer This plan has been followed by R¹e¹ Ransom²⁰ and Collier⁴ in the majority of their cases

We have surgically treated six patients with gastrojejunocolic fistula without a death In the first patient treated by a one stage operation the fistula was disconnected and normal gastrointestinal continuity restored In the remaining five a preliminary colostomy was performed In each of the latter a simple loop colostomy in the ascending colon without spur formation proved satisfactory Colostomy drainage was established on the average of the fifth postoperative day by cautery colotomy The second stage the stage of definitive surgery was done six to ten weeks later The final stage the closure of the colostomy was performed on the average of four weeks after completion of the second stage

In two of the five patients treated by preliminary colostomy the fistula was disconnected and a simple restoration of gastrointestinal continuity was performed In each of these a resection and end to end anastomosis of the jejunum was necessary

In the remaining three the fistula was disconnected the openings in the jejunum and colon were closed by simple suture and a subtotal gastric resection with an antecolic gastrojejunostomy was done At the present we prefer this plan of treatment

Our recent experiences with partial vagectomy in the treatment of duodenal ulcer have been very encouraging When adequate accumulative data are obtained will this procedure prove to be the preferred method of surgical management? The application of partial vagectomy to the treatment of gastrojejunocolic fistula remains to be determined The end results following simple closure of the fistula and restoration of normal gastrointestinal continuity have been unsatisfactory The best results have been obtained with simple closure of the fistula combined with subtotal gastric resection However gastric resection subjects the patient to an increased surgical risk symptoms are relieved at the sacrifice of two-thirds or more of the stomach anemia and inability to regain weight are not infrequent postoperative problems

The ideal would be the development of a more physiologic and less destructive method of surgical treatment A suggested plan of treatment following preliminary colostomy would be the closure of the fistula combined with infradiaphragmatic partial vagectomy A gastrojejunostomy also would be necessary if an associated obstruction of the pylorus was present Whether or not partial vagectomy will approach the ideal in the treatment of gastrojejunocolic fistula we do not know However we do believe it is a logical approach to the problem and worthy of extended clinical trial

In all cases roentgenographic demonstration of the fistula was obtained following a barium enema. The fistulous communication was visualized in only three of the cases (50 per cent) after a barium meal.

The cases were classified according to the definitive surgical treatment into two groups each group containing three cases. In Group I the fistula was disconnected and a simple restoration of gastrointestinal continuity performed. In Group II the fistula was disconnected and a subtotal gastric resection was done. A preliminary ascending loop colostomy was done in two of the cases of Group I and in each of the three cases of Group II.

A follow up study was obtained in all cases. In Group I a reactivation of the original duodenal ulcer occurred two weeks, three months and four years respectively following discharge from the hospital. In each a gastric resection was subsequently performed with complete relief of symptoms over a follow up period ranging from three to four years. In Group II there has been no recurrence of symptoms in a follow up study varying from three and one half to four years.

CONCLUSIONS

In the surgical management of gastrojejunoecolic fistulas the multi stage operation described by Pfeiffer is preferred.

The first stage preliminary ascending colostomy produces a rapid and marked improvement in the general condition of the patient as manifested by immediate control of vomiting and diarrhea, improvement in appetite, gain in weight and correction of malnutrition and anemia. It permits the subsidence of the massive inflammatory reaction about the fistula thus facilitating the technical aspects of the second stage. It obviates the danger of peritoneal soiling with colon contents when the fistula is repaired.

In the second stage a disconnection of the fistula followed by a subtotal gastric resection is preferred to simple restoration of gastrointestinal continuity. Simple closure of the fistula combined with infradiaphragmatic partial vagotomy may prove of value on extended clinical trial.

Acknowledgment made to Dr. A. Isason for information completing the follow up study in Case I.

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In Group I are those cases in which the fistula was disconnected and a simple restoration of normal gastrointestinal continuity performed. Two of the three cases in this group had a preliminary ascending colostomy. In each of these cases a reactivation of the original duodenal ulcer occurred two weeks, three months, and four years respectively following discharge from the hospital. In each case a subtotal gastric resection was done two years and five months, three months, and one year respectively subsequent to recurrence of ulcer symptoms. Following gastric resection the patients remained asymptomatic over a follow up period ranging from three and one half to four years. This improvement occurred despite the free use of tobacco and alcoholic beverages and a complete disregard of the prescribed diet.

In Group II are those cases in which a subtotal gastric resection was done. In each of the three cases of this group a preliminary ascending colostomy was performed. These cases were followed three years and nine months, three years and six months, and three years and five months respectively without recurrence of ulcer symptoms. Similarly as in Group I the follow up study revealed that not one patient observed the proper diet or abstained from the use of alcohol and tobacco. Two of the patients admitted to the consumption of twenty to thirty glasses (10 ounce) of beer a day and the use of twenty to forty cigarettes daily.

A weight gain occurred in each case. The lowest gain was twenty and the highest sixty one pounds with an average gain of thirty pounds. The highest weight gain (sixty one pounds) occurred in a patient in Group II who had symptoms referable to a gastrojejunocolic fistula for six years prior to operation.

The important feature of the follow up study shows that all the patients resumed a gainful occupation and performed without difficulty a full day's work. In three the work was of a very arduous nature and the meal habits were irregular.

Our series of six cases is too small to permit one to draw conclusions. However it may prove of interest to note that in each case in which gastric resection was performed as a definitive second stage procedure (Group II) the patients remained entirely free of symptoms. Similarly those cases (Group I) in which reactivation of the original ulcer occurred following a simple restoration of normal gastrointestinal continuity remained asymptomatic following a subtotal gastric resection.

SUMMARY

Six cases of gastrojejunocolic fistula have been reported. In each case the fistula occurred as a complication of a posterior gastrojejunostomy performed for duodenal ulcer. The treatment was surgical in all cases. There were no deaths.

Intractable diarrhea and weight loss were the outstanding symptoms and were present in each case. The other symptoms in order of frequency were abdominal pain, weakness, anemia, foul smelling eructations, stercoraceous vomiting, undigested food particles in the stools, malnutrition and anorexia.

SURGICAL DRAINS MADE OF VINYL PLASTIC FILM

HENRY G. BREGENZLE MD AND PAUL GROSS MD PITTSBURGH PA

THERE are certain disadvantages to the time honored use of gutta percha as surgical drains. There is a slight tendency for the tissues to become adherent to it and hence removal may be a painful process. Gutta percha like all types of rubber tends to deteriorate with age and thereby loses tensile strength. It is this loss of tensile strength which poses the real danger of leaving fragments of the drain in a wound because they may break off during removal.

One of the vinyl plastics is commercially available as a thin soft pliable colorless semitransparent film of great tensile strength. It has been used for drains in over 100 abdominal operations in our institution during the past year with eminently satisfactory results.

This material may be boiled or autoclaved without altering its properties. Extreme heat (far above sterilization temperature) causes the film to soften and become tacky. However the physical properties return to normal on cooling. The vinyl plastic is not affected by soap water alcohol or most solvents. It is chemically inert and is not appreciably affected by age retaining its tensile strength tenacity and semitransparency. The chemical inertness also renders this material nonirritating to tissues.

The vinyl plastic film is prepared for surgical use by scrubbing with soap and water cutting into pieces of convenient size placing a thin section of gauze between each sheet to prevent adherence sterilization in the autoclave and storage in 70 per cent alcohol.

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25
26

(see the section in the Monograph mentioned in the footnote below, on frequency of complications for the method of estimating this) who reached a forward hospital alive

Type and Location of Wounds

Of the 186 patients studied 33 had peripheral wounds without fracture. These were nearly all on the extremities. Five of these were listed as having minor (less severe) wounds in this category with their major (more severe) wounds tabulated elsewhere.

There were 83 patients having peripheral wounds with fracture. Again these were nearly all extremity wounds. 15 had traumatic amputation of an extremity. In 23 cases listed in this group more important wounds are listed under other headings.

In 34 patients thoracic wounds were present. In 7 of these the thoracic wound was less important than the other wounds present.

TABLE I. TYPICAL DELAY ALONG THE EVACUATION STREAM

SOURCE AND PERIOD OF COLLECTION	NUMBER OF CASES	AVERAGE TIME FROM WOUNDING TO BATTALION AID STATION	AVERAGE TIME FROM BATTALION AID STATION TO COLLECTING COMPANY	AVERAGE TIME FROM COLLECTING COMPANY TO CLEARING STATION	AVERAGE TIME FROM CLEARING STATION TO FORWARD HOSPITAL	AVERAGE TIME FROM FORWARD HOSPITAL ENTRY TO OPERATION	AVERAGE TOTAL TIME FROM WOUNDING TO SURGERY
North of Florence Italy Sept 1944 to March 1945	100	1.09	1.30	1.98	1.41	5.38	14.40
Loano Italy April 1945	47	4.60	1.43	0.93	0.56	8.08	15.85
Via Reggio Italy March and April 1945	44	4.59	0.81	0.99	0.60	5.13	12.15

Time is expressed in hours

Of the group 56 patients had intra abdominal wounds. A total of 19 patients had thoracoabdominal wounds. One of these had separate wounds of the chest and abdomen. Liver wounds were present in 25 absent in 160 not known in 1 patient. Wounds of the kidney were present in 20 absent in 165 and uncertain in 1 patient. In 11 of the 20 patients with kidney damage nephrectomy was done. In 10 patients wounds of the urinary tract (bladder or above) were present.

Crushing injuries were found in 9 patients. 3 had spinal cord injury.

Clinical Condition of the Patient on Arrival at the Most Forward Hospital

Pain—The frequency and severity of pain were extensively studied shortly before the Board's work was undertaken and has been described elsewhere. The types of patients observed there were similar to those considered by the Board. Part of the data obtained were as shown in Table II.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK M.D.

I THE INTERNAL STATE OF THE SEVERELY WOUNDED MAN ON ENTRY TO THE MOST FORWARD HOSPITAL

HENRY K BEECHER M.D. FIORINDO A SIMFONE M.D. CHARLES H BURNETT
M.D. SPYMOUR L SHAPIRO M.D. EUGENE R SULLIVAN M.D. AND
TRACY B MALLORY M.D. BOSTON MASS

THE effects on the human body of the destructive forces of warfare have been stated many times in terms of organic damage and tissue loss. Our concern is rather with the internal state of the wounded man. The gross tissue damage is obvious or becomes so on surgical exploration; therefore our purpose is to describe the latent consequences of the wound revealed in impairment of organic function and in abnormalities of the blood volume and chemistry and in the urine. These initial studies were made shortly after the patient entered the most forward hospital. They were made before either vigorous resuscitative measures or operation had yet been undertaken.

BACKGROUND MATERIAL

Account must be taken of the nature and type of the wound and of space and time as well for delay along the evacuation trail and the response of the patient to his wound and subsequent management all influence the factors under study and bracketed with the laboratory data give significance to them. Of the 186 seriously wounded patients studied during the course of this work 103 were examined (including blood chemistry studies) rather completely on entry to the hospital.

Evacuation Time From Wounding to Surgery

Since delay along the evacuation route may greatly influence the condition of the patient found on arrival at the most forward hospital some indication of the order of this will be given. The first 100 cases listed in Table I were chosen at random from those observed in this study during the relatively quiet part of the fall, winter and spring period. The other two batches of data are based upon casualties produced during drives. In the last period those concerned thought that considering the circumstances the evacuation to the hospital progressed exceptionally rapidly. These 191 very seriously wounded patients were the men in the worst condition drawn from about 7,000 battle casualties.

Medical Effects of Wounds
Wounded Mediterranean
do A. Smeone Henry K.
ro and Louis D. Smith
by the Government Printing
authorship

The incidence of severe pain is surprisingly low. In the report referred to, data were presented to show that the patients who had severe pain were not to be accounted for as having had less morphine or having had it longer ago than patients who reported little or no pain.

It was also pointed out that three factors are chiefly important in the distress of the wounded—pain, mental distress, and thirst. In the severely wounded patient in good general condition the first two factors are important. In the man in shock, thirst is the main, and often only, cause of evident distress, but this may be severe.

Shock—The view might be proposed in a given case that shock is either present or absent and that to try to differentiate between degrees of it is futile. Our empirical finding was, however, that it was instructive to separate the patients into four categories—no shock, slight shock, moderate shock, and severe shock.

The patients were arbitrarily divided into four groups according to the following signs, set down here because it will be useful to refer to them later in conjunction with the physiologic findings encountered.

These signs are inadequate, of course, for management of a case, because a comprehensive appraisal of the patient's condition must include not only an accurate concept of the present state of affairs, but a shrewd estimate of his probable course in the immediate future. This will be discussed in detail later. For the present, here are the arbitrary criteria for grouping the seriously wounded men (Table IIA).

On admission

	3 patients	or 1.6%	were unclassified
	34 patients	or 18.3%	were in no shock
	37 patients	or 20.0%	were in slight shock
	55 patients	or 29.5%	were in moderate shock
	57 patients	or 30.6%	were in severe shock
Total	186	100.0%	

This group includes patients who were not seen on admission by a member of the Board, but were classified on the basis of the available clinical data and on discussion with officers who had seen them. In the following group of 108 patients all were seen on admission by a member of the Board. Possibly the degree of shock was more uniformly classified here than in the other group, however the percentages are about the same in the two series.

	1 patient	or 0.9%	was unclassified
	20 patients	or 18.5%	were in no shock
	27 patients	or 25.0%	were in slight shock
	34 patients	or 31.5%	were in moderate shock
	26 patients	or 24.1%	were in severe shock
Total	108	100.0%	

Examination of the records of 167 wounded men (Table III) fails to show any correlation between time from wounding until examination (clinical ap-

TABLE II
TWO HUNDRED FIFTEEN PATIENTS WITH MAJOR WOUNDS
Standard Errors of the Mean Are Shown

TYPe OF WOUND	CONTUOUS FRACTURES OF LONG BONES	EXTENSIVE SOFT TISSUE WOUNDS	INFILTRATING WOUNDS OF FURROW	PENETRATING WOUNDS OF ABDOMEN	PENETRATING WOUNDS OF CHEST OR LIMB
Number of patients	50	50	50	50	15
Patient's age (yr)	24.8 ± 0.9	24.5 ± 1.1	24.5 ± 0.8	22.7 ± 0.0	25.1 ± 1.4
Time since wounding (hr)	12.5 ± 1.3	11.3 ± 1.4	9.9 ± 1.0	7.2 ± 0.7	7.9 ± 1.4
Average total dose of morphine (mg)	39 pts—none* 49 pts avgd 27.0 ± 1.5 22.0	11 pts—none* 39 pts avgd 27.0 ± 0.7 39.5	11 pts—none* 19 pts avgd 25.0 ± 1.8 21.2	5 pts—none* 45 pts avgd 20.0 ± 2.1 20.0	9 pts—none* 7 pts avgd 10.8 ± 1.3 10.8
Average latest dose of morphine (mg) (spread as above)					
Time since latest morphine (hr)	7.0 ± 0.8	7.2 ± 0.0	6.5 ± 0.6	4.8 ± 0.7	0.2 ± 1.5
Dose of pain (number of patients in each group)	10 none 12 slight 7 moderate 12 bad	39 none 15 slight 8 moderate 8 bad	15 none 18 slight 11 moderate 6 fatal	7 none 5 slight 14 moderate 24 bad	9 none 5 slight 0 moderate 1 bad
Further pain relief therapy wanted (no. of patients)	11 yes 39 no	9 yes 41 no	10 yes 40 no	27 yes 23 no	1 yes 14 no

*Not included in average

type of wounds (Incidentally one can see no evidence here that clostridial infection plays an important part in producing shock.)

The question might be raised as to whether the relative importance of abdominal wounds as a cause of shock in comparison with the serious extremity wounds has been exaggerated. The poor prognosis often encountered in patients with abdominal wounds probably has a great deal to do with the apprehension felt in the presence of such lesions. The concealed hemorrhage or concealed contamination often present here may lead to profound shock. Therefore, while on the average abdominal wounds may be less often a cause of severe shock on hospital entry than the serious extremity wounds the impossibility of an accurate preoperative appraisal of the abdominal wound makes it difficult to exaggerate its potentialities.

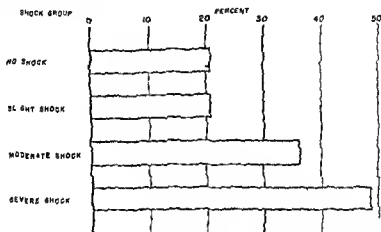


Chart 1—Incidence of serious extremity wounds in the several shock groups: traumatic amputation or compound fracture of long bones

Shock will be discussed in each of the following sections. For example see particularly the section on Blood Loss. An attempt will be made in all cases to correlate degree of shock with the data under discussion. This of course will not always be possible.

The Cardiovascular System—The material on the cardiovascular system is discussed at this point rather than before the immediately preceding section on shock, since we wish to arrange the findings when possible in terms of the several shock groups referred to there.

Electrocardiographic observations—Fifty eight records were made of 30 patients in the severe-shock group during shock and after recovery. This study was made before the Board was organized by Burnett Bland and Beecher² but since the observations were made upon the same type of patients as those studied by the Board and under similar circumstances a brief note will be inserted here as to the results found.

In 10 of the patients one third of this group the blood pressure could not be measured on entry. In the other two-thirds the degree of circulatory collapse

TABLE II A GRADING OF SHOCK*

DEGREE OF SHOCK	BLOOD PRESSURE (APPROX)	PULSE QUALITY	SKIN			THIRST	MENTAL STATE
			TEMPERATURE	COLOR	CIRCULATION (RESPONSE TO PRESSURE BLANCHING)		
None	Normal	Normal	Normal	Normal	Normal	Normal	Clear and distressed
Slight	To 20% decrease	Normal	Cool	Pale	Definite slowing	Normal	Clear and distressed
Moderate	Decrease 1 to 20 to 40%	Definite decrease in volume	Cool	Pale	Definite slowing	Definite	Clear and some apathy unless stimulated
Severe	Decreased 40% to non recordable	Weak to imperceptible	Cold	Ashen to cyanotic (not ting)	Very sluggish	Severe	Apathetic to comatose, little distress except thirst

praisal and blood analysis) and the severity of shock. The time elapsed in each of the four groups is the same. There is, however, a striking correlation of shock severity with blood loss, as shown elsewhere.

Table IV shows the wound composition of each of the shock groups (see also Table V). It merits some comment. If the patients with traumatic amputation of extremities are added to those having compound fractures of long bones, cases often very similar as far as blood loss goes, one can see (Chart 1) a sharp rise of incidence of these cases as one deals with groups of patients in increasingly poor condition.

In the section on blood loss it will be shown that the greatest loss of hemoglobin occurs in wounds that involve compound fractures of long bones or traumatic amputation. Since these wounds are most prevalent in the severe shock group, one can generalize with probability of accuracy and say that it is the wounds that are associated with great hemorrhage that cause the severe shock. Reasons for laboring this rather obvious point will be discussed later.

In contrast to the rising incidence of the severe extremity wounds just referred to, the percentage of penetrated abdomens, although rather high, shows no consistent rise in the four groups. In the severe shock group, abdominal wounds are definitely less often a cause of the poor condition than the other

TABLE III RELATIONSHIP OF DEGREE OF SHOCK ON HOSPITAL ARRIVAL TO TIME FROM WOUNDING

DEGREE OF SHOCK	NONE	SLIGHT	MODERATELY SEVERE	SEVERE
Time from wounding to hospital entry (hours)	67 ± 09 (29 cases)	76 ± 04 (36 cases)	61 ± 05 (102 cases)	64 ± 07 (50 cases)

Standard errors of the mean are shown

TABLE V

CONDITION OF THE PATIENT	INCIDENCE OF TRAUMATIC AMPUTATION OR COMPOUND FRACTURE OF LONG BONES	
	(PER CENT)	
No shock	20.8	
Slight shock	20.8	
Moderate shock	36.1	
Severe shock	48.6	

was somewhat less severe but even so the systolic blood pressures were 60 to 70 mm Hg and the diastolic 20 to 40. Definite abnormalities of the electrocardiograms were observed in 5 of the 30 patients. The most striking feature was the normal character of the remaining 25 patients.

Of the 5 patients with abnormal electrocardiograms 2 showed striking but transient inversion of the T wave in Lead I. In a patient with intrathoracic injury there was a shift from marked right axis deviation back to normal following operation. Another patient showed bizarre QRS complexes of low voltage and the final patient exhibited an unusual degree of temporary cardiac irritability with paroxysmal fibrillation and ventricular tachycardia.

The abnormalities in the electrocardiograms are of some interest and difficult to explain. In no instance did we observe clinical signs of cardiac weakness in the form of abnormal accentuation of the pulmonary second sound, basal rales, gallop rhythm or congestion of the cervical veins or of the liver. As remarked previously, the majority of the electrocardiograms were normal in character. Several patients in the series were in severe shock with low blood pressures for a period of hours with no effect upon the electrocardiogram. It may be significant that in both patients with the transient inversion of the T waves in Lead I the wound involved the left side of the chest although as far as could be determined by x-ray examination and at the time of operation the heart and pericardium escaped injury. Furthermore the transient nature of the inversion was more in accord with a temporary functional disturbance (possibly hypoxia) than with lasting tissue injury.

The pulse rate. There was no significant difference in rate between the four groups (Table VA). The pulse rates were taken as near as possible to the time the condition of the patient was evaluated. When it was imperceptible the next recorded pulse rate was taken unless the record showed evidence that the case was resuscitated or nearly so.

The finding that the average as well as minimum and maximum pulse rates were the same in all degrees of shock was surprising. This is explained in two ways: (1) the tachycardia in the lesser degrees of shock may have been due in

TABLE VA THE PULSE RATE IN DIFFERENT DEGREES OF SHOCK

DEGREE OF SHOCK	NONE (13 CASES)	SLIGHT (24 CASES)	MODERATELY SEVERE (34 CASES)	SEVERE (30 CASES)
Minimum pulse rate	70	88	80	70
Maximum pulse rate	140	150	160	144
Average	103 ± 2	111 ± 3.4	113 ± 3.6	116 ± 3.3

TABLE IV. ONE HUNDRED TWENTY-ONE PATIENTS CLASSIFIED AS TO DEGREE OF LOCK ON ADMISSON WITH CUT WOUND COMPOSITION OF FRACTURE

1 Q F P R CCK	NUM FL CLASS BIP	IFNL F ATT A M FN	PIN LAT D C FT	ACRYL D FON P T SALT	TRAUMATO AL TA TON OF	COM BOUND FRAC RE OF LONG IONS	3. SCULPTOR S	EXPLANATION
None	01	7	1	0%	3	1	7 er 1	1 1

*100% in case not incl. 0% to 100% in case not incl. 0% to 100% in case not incl.

CASE 1 (No 77)—The patient had a severe thoracoabdominal wound. He was received at a forward hospital in severe shock eight hours and fifteen minutes after wounding. Resuscitation was continued for nearly nine hours. During that time he received only 1,500 cc of blood. His condition failed to improve and he was operated upon, but did not survive the operation. Autopsy showed massive collapse of the right lung with a plug of mucus in the right main bronchus. The lower lobe of the left lung was collapsed and about one third of the left upper lobe was atelectatic. There was gross dilatation of the right ventricle of the heart. Histologically, minimal evidence of fat embolism in the pulmonary vessels was found but thought to be of no clinical significance.

Comment There was adequate cause for the failure of this patient to respond to resuscitation. More aggressive measures should have been taken, including bronchoscopy and the use of more blood in less time. There should have been more concern when little improvement was seen during the first three hours after admission to the hospital.

CASE 2 (No 45)—The patient had a severe abdominal wound and was admitted in severe shock to a forward hospital eight hours after wounding. During the next three hours, two units (600 cc) total volume of plasma and one liter of blood were transfused. The blood pressure during that time changed from imperceptible to 90 systolic and 70 diastolic. He was given 300 cc more of plasma and 500 cc of 2 per cent sodium bicarbonate solution intravenously. This was the optimum time for surgery. Operation was delayed, however, and five hours later, the blood pressure was again unmeasurable. It was restored to 86 systolic and 60 diastolic after one liter of blood, and operation was performed, which lasted four hours. At operation the abdominal cavity was found 'full of blood'. The blood pressure and pulse were unmeasurable during much of the operation. The patient did not regain consciousness and died three and three quarters hours after the end of the operation. Autopsy showed a perforation of the inferior vena cava. There was evidence of minimal fat embolism in the pulmonary vessels histologically, probably of no clinical significance.

Comment The recurrent hypotension in this patient was probably due to continued extraperitoneal and intraperitoneal hemorrhage. Operation should have been performed when he showed good response to resuscitation during the first three hours after admission to the hospital.

CASE 3 (No 100)—The patient had multiple wounds involving both arms, the left thigh, and the face. There were compound fractures of the left humerus, radius, and ulna, and of the right ulna. He also had a transection of the right femoral artery with vascular insufficiency in the leg. He was admitted in severe shock to a forward hospital three and one half hours after wounding. Within ninety minutes the patient received 300 cc of plasma and two liters of blood. He showed improvement but the blood pressure was still only 80 systolic and 50 diastolic. The pulse was 144. Three hours after admission the blood pressure was 90/58. Operation was delayed for three more hours. During operation the recorded blood pressure never fell below 85 mm Hg systolic. Before, during and after operation he received 4,500 cc blood and ten hours after operation he had hypotension and looked pale and 'anemic'. A transfusion was started. One hour later the patient suddenly died. Ten minutes earlier he had carried on an intelligent conversation. Pulmonary embolism was suspected but at autopsy no cause could be found for the sudden death. Microscopically, a moderately severe grade of fat embolism was found in the lungs. It may well have contributed to the unexpected death of the patient.

Comment The question was asked if the five or six hour period of hypotension in this patient could have caused irreversible changes in the cardio

part to excitement and (2) in some cases the elevation in the pulse rate (and the vasoconstriction accompanying it) may have been adequate to ward off the signs of shock. It is interesting that even patients judged to be in severe shock can have a pulse rate as low as 60 per minute. In such a case other factors clearly outweighed this one in grading the shock. Of greater significance than the actual rate of pulse is its volume which often is decreased so far in severe shock that the pulse can no longer be felt.

The blood pressure. The blood pressures were analyzed only for those cases where they were recorded at the time the condition of the patient was evaluated. There were 70 such cases and the circulating blood volume was determined in all of them.

A significant fall in the systolic blood pressure did not occur until the group considered to be in moderately severe shock was reached (Table VB). These patients had lost 33.6 ± 3.2 per cent of their calculated normal blood volumes and nearly 50 per cent of the total circulating hemoglobin. With more severe degrees of shock the systolic blood pressure fell more rapidly. The (average) systolic blood pressure in severe shock was 49 ± 7.6 mm Hg. This group had lost approximately one half the calculated normal blood volume.

Table VB shows a progressive drop in the diastolic blood pressure with increasing degrees of shock. The average diastolic blood pressure of patients in severe shock is one half that of patients in moderate shock.

As the severity of shock increases there is a significant and progressive decline in the pulse pressures (Table VB). This fits the clinical observation that the volume of the pulse is closely correlated with the degree of shock.

TABLE VB THE BLOOD PRESSURE IN RELATION TO DEGREE OF SHOCK

DEGREE OF SHOCK								BLOOD PRESSURE	
								HIGH	LOW
								EST	ATRIAL
None								8	5-41
(13 cases)	90	140	100 ± 3.0	40	86	66 ± 7.7	93	80	44 ± 7
Mild									
(20 cases)	30	136	95 ± 4.9	20	90	59 ± 3.5	10	56	36 ± 9
Moderate									
(21 cases)	0	90	49 ± 7.6	0	64	35 ± 5.5	0	59	24 ± 4.7
Severe									
(16 cases)									

*Where the values were unmeasurable (2 cases) they were considered to be 0.

"Irreversible" changes in the cardiovascular system. Everyone dealing

with shock has observed that the failure of response is often attributed to the supposition that "irreversible" changes have taken place during prolonged hypotension, ischemia and anoxia. This is discussed also in the section on Blood Loss. In most instances adequate explanation is found for the failure of patients in shock to respond to transfusion, some common examples are concealed and continuing hemorrhage, hemothorax, irritant contamination of the peritoneum, peritonitis, clostridial myositis and fat emboli. Four typical cases are presented.

CASE 1 (No 77) —The patient had a severe thoracoabdominal wound. He was received at a forward hospital in severe shock eight hours and fifteen minutes after wounding. Resuscitation was continued for nearly nine hours. During that time he received only 1,500 cc of blood. His condition failed to improve and he was operated upon, but did not survive the operation. Autopsy showed massive collapse of the right lung with a plug of mucus in the right main bronchus. The lower lobe of the left lung was collapsed and about one third of the left upper lobe was atelectatic. There was gross dilatation of the right ventricle of the heart. Histologically, minimal evidence of fat embolism in the pulmonary vessels was found, but thought to be of no clinical significance.

Comment: There was adequate cause for the failure of this patient to respond to resuscitation. More aggressive measures should have been taken, including bronchoscopy and the use of more blood in less time. There should have been more concern when little improvement was seen during the first three hours after admission to the hospital.

CASE 2 (No 45) —The patient had a severe abdominal wound and was admitted in severe shock to a forward hospital eight hours after wounding. During the next three hours, two units (600 cc) total volume of plasma and one liter of blood were transfused. The blood pressure during that time changed from imperceptible to 90 systolic and 70 diastolic. He was given 300 cc more of plasma and 500 cc of 2 per cent sodium bicarbonate solution intravenously. This was the optimum time for surgery. Operation was delayed, however, and six hours later, the blood pressure was again unmeasurable. It was restored to 86 systolic and 60 diastolic after one liter of blood, and operation was performed, which lasted four hours. At operation the abdominal cavity was found "full of blood." The blood pressure and pulse were unmeasurable during much of the operation. The patient did not regain consciousness and died three and three quarters hours after the end of the operation. Autopsy showed a perforation of the inferior vena cava. There was evidence of minimal fat embolism in the pulmonary vessels histologically, probably of no clinical significance.

Comment: The recurrent hypotension in this patient was probably due to continued extraperitoneal and intraperitoneal hemorrhage. Operation should have been performed when he showed good response to resuscitation during the first three hours after admission to the hospital.

CASE 3 (No 100) —The patient had multiple wounds involving both arms, the left thigh, and the face. There were compound fractures of the left humerus, radius, and ulna, and of the right ulna. He also had a transection of the right femoral artery with vascular insufficiency in the leg. He was admitted in severe shock to a forward hospital three and one half hours after wounding. Within ninety minutes the patient received 300 cc of plasma and two liters of blood. He showed improvement but the blood pressure was still only 80 systolic and 50 diastolic. The pulse was 144. Three hours after admission the blood pressure was 90/58. Operation was delayed for three more hours. During operation the recorded blood pressure never fell below 85 mm Hg systolic. Before, during, and after operation, he received 4,500 cc blood, and ten hours after operation he had hypotension and looked pale and "anemic." A transfusion was started. One hour later the patient suddenly died. Ten minutes earlier he had carried on an intelligent conversation. Pulmonary embolus was suspected, but at autopsy no cause could be found for the sudden death. Microscopically, a moderately severe grade of fat embolism was found in the lungs. It may well have contributed to the unexpected death of the patient.

Comment: The question was asked if the five- or six hour period of hypotension in this patient could have caused irreversible changes in the cardio

part to excitement and (2) in some cases the elevation in the pulse rate (and the vasoconstriction accompanying it) may have been adequate to ward off the signs of shock. It is interesting that even patients judged to be in severe shock can have a pulse rate as low as 60 per minute. In such a case other factors clearly outweighed this one in grading the shock. Of greater significance than the actual rate of pulse is its volume which often is decreased so far in severe shock that the pulse can no longer be felt.

The blood pressure The blood pressures were analyzed only for those cases where they were recorded at the time the condition of the patient was evaluated. There were 70 such cases and the circulating blood volume was determined in all of them.

A significant fall in the systolic blood pressure did not occur until the group considered to be in moderately severe shock was reached (Table VB). These patients had lost 33.6 ± 3.2 per cent of their calculated normal blood volumes and nearly 50 per cent of the total circulating hemoglobin. With more severe degrees of shock, the systolic blood pressure fell more rapidly. The (average) systolic blood pressure in severe shock was 49 ± 7.6 mm Hg. This group had lost approximately one half the calculated normal blood volume.

Table VB shows a progressive drop in the diastolic blood pressure with increasing degrees of shock. The average diastolic blood pressure of patients in severe shock is one half that of patients in moderate shock.

As the severity of shock increases there is a significant and progressive decline in the pulse pressures (Table VB). This fits the clinical observation that the volume of the pulse is closely correlated with the degree of shock.

TABLE VB THE BLOOD PRESSURE IN RELATION TO DEGREE OF SHOCK

DEGREE OF SHOCK	PULSE PRESSURE							
	LOW EST			HIGH EST			AVERAGE	
	9)	8)	7)	6)	5)	4)	3 + 4)	
None (13 cases)								
Slight (20 cases)	40	140	109 ± 3.0	49	96	65 ± 7.7	88	41 ± 7.7
Moderate (21 cases)	30	136	85 ± 4.9	70	90	59 ± 3.5	10	36 ± 7.8
Severe (16 cases)	0	80	49 ± 7.6	0	69	25 ± 5.8	0	21 ± 4.4

Where the values were unmeasurable (cases) they were considered to be 0.

"Irreversible" changes in the cardiovascular system Everyone dealing with patients in shock has the problem of the patient who fails to respond to the transfusion of blood thought adequate under ordinary circumstances. The failure of response is often attributed to the supposition that irreversible changes have taken place during prolonged hypotension, ischemia and anoxia. This is discussed also in the section on Blood Loss. In most instances adequate explanation is found for the failure of patients in shock to respond to transfusion; some common examples are concealed and continuing hemorrhage, hemothorax, irritant contamination of the peritoneum, peritonitis, clostridial myositis and fat emboli. Four typical cases are presented.

CASE 1 (No 77)—The patient had a severe thoracoabdominal wound. He was received at a forward hospital in severe shock eight hours and fifteen minutes after wounding. Resuscitation was continued for nearly nine hours. During that time he received only 1,500 cc of blood. The operation the night man of the left upper lobe was atelectatic. There was gross dilatation of the right ventricle of the heart. Histologically, minimal evidence of fat embolism in the pulmonary vessels was found, but thought to be of no clinical significance.

Comment. There was adequate cause for the failure of this patient to respond to resuscitation. More aggressive measures should have been taken, including bronchoscopy and the use of more blood in less time. There should have been more concern when little improvement was seen during the first three hours after admission to the hospital.

CASE 2 (No 45)—The patient had a severe abdominal wound and was admitted in severe shock to a forward hospital eight hours after wounding. During the next three hours, two units (600 cc) total volume of plasma and one liter of blood were transfused. The blood pressure during that time changed from imperceptible to 90 systolic and 70 diastolic. He was given 300 cc more of plasma and 500 cc of 2 per cent sodium bicarbonate solution intravenously. This was the optimum time for surgery. Operation was delayed, however, and five hours later, the blood pressure was again unmeasurable. It was restored to 80 systolic and 60 diastolic after one liter of blood, and operation was performed, which lasted four hours. At operation the abdominal cavity was found "full of blood." The blood pressure and pulse were unmeasurable during much of the operation. The patient did not regain consciousness and died three and three quarters hours after the end of the operation. Autopsy showed a perforation of the inferior vena cava. There was evidence of minimal fat embolism in the pulmonary vessels histologically, probably of no clinical significance.

Comment. The recurrent hypotension in this patient was probably due to continued extraperitoneal and intraperitoneal hemorrhage. Operation should have been performed when he showed good response to resuscitation during the first three hours after admission to the hospital.

CASE 3 (No 100)—The patient had multiple wounds involving both arms, the left thigh, and the face. There were compound fractures of the left humerus, radius, and ulna, and of the right ulna. He also had a transection of the right femoral artery with vascular insufficiency in the leg. He was admitted in severe shock to a forward hospital three and one half hours after wounding. Within ninety minutes the patient received 300 cc of plasma and two liters of blood. He showed improvement but the blood pressure was still only 80 systolic and 50 diastolic. The pulse was 144. Three hours after admission the blood pressure was 80/54. Operation was delayed for three more hours. During operation the recorded blood pressure never fell below 85 mm Hg systolic. Before, during and after operation, he received 4,500 cc blood and ten hours after operation he had hypotension and looked pale and anemic. A transfusion was started. One hour later the patient suddenly died. Ten minutes earlier he had carried on an intelligent conversation. Pulmonary embolus was suspected, but at autopsy no cause could be found for the sudden death. Microscopically, a moderately severe grade of fat embolism was found in the lungs. It may well have contributed to the unexpected death of the patient.

Comment. The question was asked if the five- or six-hour period of hypotension in this patient could have caused irreversible changes in the cardio-

vascular system so that it simply "gave out" when it did. The question can not be answered with certainty. The fat embolism, in retrospect appears to be the more important consideration.

CASE 4 (No 120)—The patient had a simple penetrating wound of the thigh caused by a shell fragment. The femoral artery below the origin of the profunda femoris was severed. During evacuation he received four units of plasma and when he reached the evacuation hospital, about nine hours after wounding, he must have appeared in good condition for no resuscitation was thought necessary, and operation was performed four and one half hours after admission. The femoral artery, vein, and nerve were found completely transected. The vessels were ligated and the foreign body was removed. At the close of the operation, the blood pressure was only 70 mm Hg and remained between 70 and 60 throughout the day. In spite of this, the patient seemed to have good color and the skin was not cold. One liter of blood did not improve the blood pressure. The right leg looked as though it would not survive. The patient developed anemia and died forty eight hours after operation. Autopsy showed nothing to account for the hypotension postoperatively. There was no concealed hemorrhage and no evidence of electrical myositis in the involved extremity. There was no evidence of fat embolism histologically.

Comment. This patient, no doubt, had lost more blood than was realized at the time he was admitted to the hospital.

Resuscitation

The principles on which resuscitation was carried out, as well as the routine procedures involved in caring for the typical patient, have been described in a section of the Appendix of the Monograph mentioned in the footnote, page 672.

In the 108 patients who were fairly completely studied shortly after their hospital entry, resuscitative efforts had been limited chiefly to control of pain (see Monograph) and hemorrhage, and administration of plasma. Only a relatively little blood was administered, this is described forthwith. These 108 patients had, on the average, two units of plasma before the first blood sample was taken divided as follows:

32	had	no	plasma
25	had	1	unit
17	had	2	units
13	had	3	units
12	had	4	units
3	had	5	units
1	had	6	units
1	had	7	units
2	had	8	units
1	had	9	units
1	had	11	units

Total 108

Blood administration prior to withdrawal from the patient of the first blood specimen for laboratory analysis was spread out as follows in the 27 patients of the 108 who were given whole blood under these circumstances:

13, or 12%, received $\frac{1}{2}$ to 1 unit (500 cc.)

10, or	9%	received	1½ to 2 units
2, or	2%	received	3 units
1, or	1%	received	4 units
1, or	1%	received	6 units

Three of these, or 3 per cent received blood in an aid station, before admission to a forward hospital. Thus 70 per cent of these very seriously wounded patients had had two units or less of plasma on arrival at the most forward hospital.

A summary of the average quantities of blood and of blood plasma used in resuscitating 154* of the very seriously wounded patients studied in our series is as follows:

Preoperative blood plasma	308 units	(average of 122 cases)
Blood plasma given during operation	168 units	(average of 10 cases)
Preoperative blood	1450 cc	(average of 127 cases)
Blood given during operation	1160 cc	(average of 95 cases)

In round numbers our average patient had just over three units blood plasma and five blood transfusions to support him from the time of wounding until the operation was completed. It is interesting to observe that plasma was used during surgery in only 10 of these 154 patients.

The information concerning the cases referred to here was drawn from the shock tents of most of the hospitals of the Fifth Army and represents a broad sample of current practice in Italy over the last year of the European War. Essentially the same type of case was studied by Beecher and Burnett³ at Anzio. In that study the average patient received 1537 cc blood (three transfusions) to prepare him for and carry him through surgery. These three transfusions contrast with the five referred to previously. A notable difference between the Anzio study and Theater practice as a whole is in the time elapsed from hospital entry to start of surgery. In the Anzio study this averaged two hours and twenty one minutes. Reference to the earlier part of this section on Evacuation Time From Wounding to Surgery will show that over the Army area as a whole the time from hospital entry to surgery varies from an average of five hours to an average of eight hours. Two differing views as to the correct preparation of wounded men for surgery are represented in these figures: the extended or the rapid. The extended required five transfusions of whole blood, the rapid three. This has been discussed in detail elsewhere.⁴

PLASMA PROTEIN AND HEMOGLOBIN LEVELS ON FORWARD HOSPITAL ADMISSION

Consideration of plasma protein and hemoglobin levels (determined by the copper sulfate method⁵) gives a clue to the shifts that have taken place between the blood stream and the tissues (or loss into the outside world). When considered with quantitative measurements of whole blood loss, a fairly accurate picture of one consequence of the wound can be obtained.

*This number includes the 10% patients just referred to. In order to get as large a sample as possible 49 others are added on whom we had clinical notes but did not have the admission blood chemistry data that characterized the group of 154.

Excluding the crush cases 50 patients are shown in Table VI that had before study, one unit* of plasma or less. These were considered shortly after their admission to the most forward hospital, before resuscitation anesthesia or operation had been undertaken

Relationship of Plasma Protein and Hematocrit to Type of Wound

From Table VI it can be seen that there is no decided difference between the plasma protein levels in the two groups of wounds described there. On the other hand the hematocrit values appear significantly higher in the abdominal group, in the direction of the hemoconcentration often found in this group. The hemoglobin loss (see the following section on Blood Loss) is smaller in the abdominal wound group than in wounds of the extremities. Maintenance of a blood volume nearer normal in the abdominal cases doubtless reduces the need and tendency for blood dilution, although of course this alone would not account for the hemoconcentration often found with the abdominal wounds.

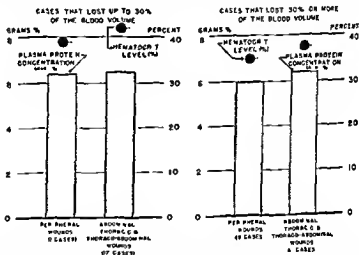


Chart 2.—Plasma protein concentration and hematocrit value in relation to type of wound and degree of blood loss. Patients received only 0 to 1 units of plasma before determination

Relationship of Plasma Protein and Hematocrit to Blood Loss

In 40 of the 43 soldiers considered here the blood loss was measured (See Table VII and Chart 2). There is a significantly lower hematocrit (All Cases) when more than 30 per cent of the calculated normal blood volume has been lost than otherwise. The 36.0 per cent hematocrit is 23.4 per cent below the normal of 47. The fact has been observed that in the case of the plasma proteins, even when there is a loss of 30 per cent or more of the normal blood volume, the plasma protein concentration is 6.1 Gm per cent (6.1 per cent below normal, 6.5 Gm per cent). In other words the hematocrit falls proportionately about four times as much as the plasma proteins. The blood appears to have been diluted by protein rich (6.1 Per cent) fluid. Where can this have

*The equivalent of 250 c.c. normal plasma diluted to 300 c.c.

TABLE VI COMPARISON OF ABDOMINAL WITH PERIPHERAL WOUNDS*

WOUNDS	PLASMA PROTEIN (GRAMS PER CENT)	HEMATOCRIT (PER CENT CELLS)
Peripheral (25 cases)	62±0.1	37.4±1.0
Abdominal (25 cases)	65±0.1	42.0±1.0

plasma before determination excludes crush

come from? The evidence is too meager to justify much speculation here. However as pointed out by Robley Evans the axial stream of corpuscles is surrounded by a plasma envelope. This varies in thickness (and total volume) depending on certain hydraulic principles. Is it possible that the alterations in the circulation caused by the loss of 30 per cent or more of the normal volume (slowing of the peripheral circulation for example) result in throwing an appreciable volume of plasma (with normal protein content) into the circulating blood?

Possibly protein may be brought into the circulation from the liver.

TABLE VII PLASMA PROTEIN CONCENTRATION AND HEMATOCRIT VALUE IN RELATION TO TYPE OF WOUND AND DEGREE OF BLOOD LOSS

Patients Received only 0 to 1 Unit of Plasma Before Determination

WOUNDS	PATIENTS WHO LOST UP TO 30% OF THE BLOOD VOLUME			PATIENTS WHO LOST 30% OR MORE OF THE BLOOD VOLUME		
	PERIPH- ERAL WOUNDS (10 CASES)	ABDOMINAL THORACIC AND THORACO ABDOMINAL WOUNDS (17 CASES)	ALL CASES (27 CASES)	PERIPH- ERAL WOUNDS (8 CASES)	ABDOMINAL THORACIC AND THORACO ABDOMINAL WOUNDS (4 CASES)	ALL CASES (12 CASES)
Plasma protein con- centration	64±0.1	65±0.1	65±0.1	60±0.1	64	61±0.1
Hematocrit level	39.0±1.7	43.0±1.0	41.5±1.0	39.0±1.3	37.8	36.0±1.1

*Influence of Plasma Therapy Upon Plasma Protein and Hematocrit
(Before the Determinations Were Made)*

Only 3 of the 55 cases shown in Table VIII had included blood transfusions. These will be ignored. It is clear that the plasma protein level is not influenced by the plasma therapy (see Chart 3). But this has an important

TABLE VIIIA HEMATOCRIT AND PLASMA PROTEIN LEVELS IN ABDOMINAL WOUNDS (EXCLUSIVE OF CRUSH SYNDROME)

Values Upon Admission to Hospital Average and Standard Errors of the Mean

WOUNDS	Values Upon Admission to Hospital		Average and Standard Errors of the Mean	
	(54 cases)	(24 cases)	(54 cases)	(24 cases)
Shock and Moderate and Severe Shock.	The data in this table were also broken down into two further groups: None and Slight Shock, and Moderate and Severe Shock. No differences were found, so these data have been omitted.			

effect (or at least accompanies the condition which required the increasing volumes of plasma) on the hematocrit (see also Tables VIIIA, VIIIB, and Chart 4) The plasma protein, hematocrit, and time after wounding were analyzed in regard to shock, the data being broken up into two groups where no shock and slight shock were grouped together, as were moderate and severe shock. No important differences were found between the two groups

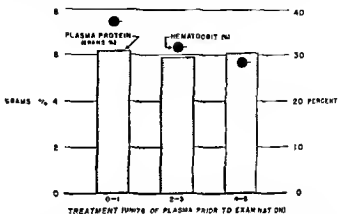


Chart 3—Hematocrit and plasma protein levels peripheral wounds exclusive of crush syndrome values upon admission to hospital average. Note that the data in the table were also broken down into two further groups: none and slight shock and moderate and severe shock. No differences were found so these data have been omitted.

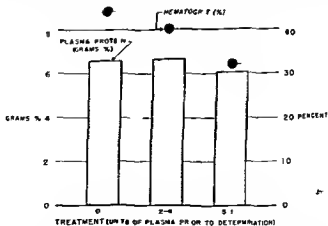


Chart 4—Hematocrit and plasma protein levels abdominal wounds values upon admission to hospital averages

TABLE VIII. HEMATOCRIT AND PLASMA PROTEIN LEVELS IN ABDOMINAL WOUNDS
Values Upon Admission to Hospital Averages and Standard Errors of the Mean

TREATMENT (UNITS OF PLASMA PRIOR TO DETERMINATION)	HEMATOCRIT (%)	PLASMA PROTEIN (GRAMS %)	HOURS AFTER WOUNDING
0 to 1 (11 cases)	41.1 ± 1.8	66 ± 0.2	6.3 ± 1.4
2 to 4 (5 cases)	40.2 ± 4.3	67 ± 0.3	7.8 ± 1.1
5 to 11	39.2 (2 cases)	61 (3 cases)	12.2 (2 cases)
Total	41.0 ± 1.3 (19 cases)	66 ± 0.1 (19 cases)	6.8 ± 1.3 (16 cases)

TABLE VIII. HEMATOCRIT AND PLASMA PROTEIN LEVELS IN THORACIC WOUNDS
Admission Values Averages and Standard Errors of Means

0 to 1 (7 cases)	66 ± 0.2	35.4 ± 1.8	7.2 ± 1.7
Total (15 cases)	65 ± 0.1	37.8 ± 1.2	7.6 ± 1.4

Relationship of Plasma Protein and Hematocrit to Degree of Shock

The plasma protein and hematocrit levels were considered with regard to their clinical condition in 100 badly wounded patients on admission to the forward hospital (crush cases excluded) (see Table IX and Chart 5). The fall in plasma protein is probably significant as the cases are grouped here the fall in hematocrit is definitely significant. No sign of hemoconcentration is present here. When the cases are divided according to location of wound there is no significant fall in plasma protein in the peripheral wounds with relation to degree of shock. The abdominal wounds show up differently (see Table X and Chart 6).

TABLE IX. AVERAGE HEMATOCRIT AND PLASMA PROTEIN LEVELS IN DIFFERENT DEGREES OF SHOCK (ADMISSION VALUES)

All Types of Cases Exclude of Crush Syndrome

FACTOR	NO SHOCK (15 CASES)	SLIGHT SHOCK (26 CASES)	MODERATE SHOCK	SEVERE SHOCK	TOTAL
Plasma protein Grams %	66 ± 0.1	64 ± 0.1	6 ± 0.1 (34 cases)	60 ± 0.1 (25 cases)	63 ± 0.1 (100 cases)
Hematocrit (%)	40.5 ± 1.7	39.4 ± 1.5	34.6 ± 1.0 (33 cases)	31.5 ± 1.5 (24 cases)	36.1 ± 0.8 (99 cases)

In the no shock-slight shock group the plasma concentration is possibly to be accounted for by weeping of the irritated peritoneal surfaces fluid being released which contains less protein than that of the plasma. As shock becomes moderate or severe probably due to greater blood loss the plasma protein falls to a figure like that for extremely wounds with hemodilution overcoming the effects of exudation.

effect (or at least accompanies the condition which required the increasing volumes of plasma) on the hematocrit (see also Tables VIIIA, VIIIB, and Chart 4). The plasma protein, hematocrit, and time after wounding were analyzed in regard to shock, the data being broken up into two groups where no shock and slight shock were grouped together, as were moderate and severe shock. No important differences were found between the two groups.

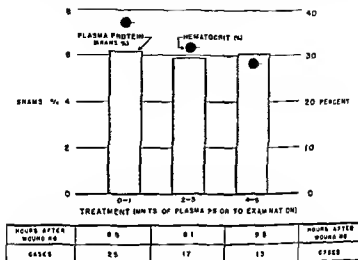


Chart 3.—Hematocrit and plasma protein levels peripheral wounds exclusive of crush syndrome values upon admission to hospital average. Note that the data in the table were also broken down into two further groups none and slight shock and moderate and severe shock. No differences were found so these data have been omitted.

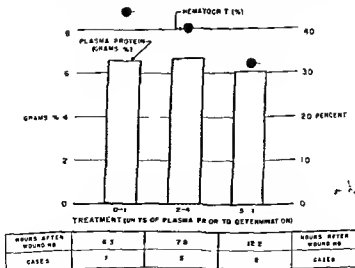


Chart 4.—Hematocrit and plasma protein levels abdominal wounds values upon admission to hospital average.

TABLE X ABDOMINAL WOUNDS HOSPITAL ADMISSION DATA

	DEGREE OF SHOCK	
	NONE TO SLIGHT	MODERATE TO SEVERE
Plasma prote n (Grams %)	69+01 (10 cases)	61+0 ~ (9 cases)
Hematoer t (% cells)	470+16 (10 cases)	349+18 (8 cases)
Hours after wounding	70+15 (10 cases)	116+32 (9 cases)

Data have been presented which indicate that the plasma protein and hematocrit values can vary independently

BLOOD LOSS (VOLUME AND HEMOGLOBIN)

The quantity of blood a wounded man can lose and yet recover has generally been underestimated. One reason for this is the fact well shown in the prolonged campaigns of the Mediterranean Theater that robust young soldiers will tolerate surgery well long before their blood volume or even blood pressure has been restored to normal. (The concept of restoration of the shocked man to normal as a preliminary to surgery is based upon a false premise. Full or game restoration probably takes up to days to achieve.) A good response of a young wounded man to treatment is by no means admissible evidence that the circulatory system has been restored to normal. There is a great factor of safety here. These points have been discussed elsewhere*.

In the belief that an accurate measurement of the blood loss of wounded men as they arrive at the most forward hospital would emphasize the importance of whole blood administration to the wounded such studies were carried out. In addition to this practical point the results have shown in a useful way the almost quantitative relationship between blood loss and degree of shock long recognized but always in need of all the support possible in order to outride the ever recurring storms arising from suggestions that the cause of shock is mysterious and to be explained by toxins or the breakdown of some vague but vital force.

The degree of wound shock as we saw it in men injured in battle precisely paralleled the blood loss. Conversely clinical recovery from shock resulted promptly from the administration of whole blood. Although we made intensive search at the bedside of thousands of wounded men throughout the shock tents of Italy we never found a clear case of irreversible shock so easily spoken of in published articles on this subject. To be sure we were unable in the case of the soldier who had both thighs blown off just outside our tent by a shell burst at Anzio to get blood into him fast enough to save his life. He died in a very few minutes. Nor were we able to resuscitate individuals who had been so long without circulation in the central nervous system that nearly all centers appeared to be dead except the respiratory. We were not able to overcome death of organs or of nervous tissue by resuscitative effort. But to apply the term irreversible shock to either type of case is to use a definition that we believe has no place at the bedside however interesting it may be as a concept a con-

*See the section on 'Resuscitation' in the Appendix of the Monograph mentioned in the footnote, page 472.

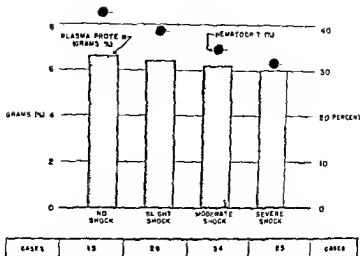


Chart 3.—Average hemoglobin and plasma protein levels in different degrees of shock admission levels all types of cases exclusive of crush syndrome

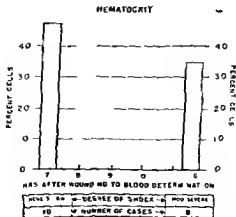
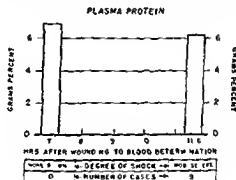


Chart 4.—Abdominal wounds (hospital) admission data

body weight) in each case. In the case of total hemoglobin, loss corrections "A" and "B" are essentially the same because, with rare exceptions, blood was not administered before the patient reached the forward hospital and the blood volume measured. See Tables XA, XB, XC, XD, XE, XF and XG.

TABLE XC SLIGHT SHOCK (20 CASES)

CASE NUMBER	BLOOD VOLUME CHANGE (% OF NORMAL)			TOTAL HEMOGLOBIN CHANGE (% OF NORMAL)			BLOOD PRESSURE AT TIME OF DETERMINA- TION (MM HG)	HOURS AFTER WOUND ING	BLOOD SUGAR (MG %)
	ON SERVED	CORRECTED		GR REPEATED	CORRECTED				
		A	B		A	B			
144	88*	67	15	30.0	30.6	30.6	90/62	12 1/2	-
140	168*	11	11	117*	58	58	100/60	4 1/2	141
143	84	157	121	278	307	307	100/50	9	-
141	202	235	255	317	391	391	100/60	7	131
A 23	197	223	187	151	151	151	126/80	3 1/2	140
A 26	74	74	74	231	211	211	110/70	4	106
A 40	35*	35*	35*	51	55	55	100/64	3 1/2	126
124	60*	49.8	32.6	97	39.9	39.8	110/80	6 1/2	184
127	39.8	59.4	44.2	63.1	65.9	65.9	90/40	11	-
A 17	41.5	63.0	49.0	61.6	69.1	69.1	140/80	3 1/2	201
A 20	33.0	37.9	37.9	56.6	56.6	56.6	92/50	13 1/2	145
113	14.9	20.2	20.2	21.4	28.2	28.2	94/58	3 1/2	149
111	27	71	71	51	51	51	120/80	14 1/2	157
83	131*	33	0.8	3.9	16.1	16.1	130/70	5 1/2	-
A 9	14.8	14.8	14.8	23.3	23.3	23.3	109/70	10	-
A 10	37	37	37	24.4	24.4	24.4	108/74	11 1/2	-
A 11	20.9	33.4	29.0	37.4	37.4	37.4	110/78	5 1/2	79
A 1	9.3	17.4	14.0	17.8	22.6	22.6	116/60	2 1/2	155
A 2	23	23	23	9.6	9.6	9.6	114/62	4 1/2	170
A 3	25.3	25.3	25.3	15.6	30.6	30.6	120/86	8	106

*All percentages represent decreases except those marked which represent increases

TABLE XI MODERATE SHOCK (21 CASES)

CASE NUMBER	BLOOD PRESS						BLOOD SUGAR (MG %)		
	BY THE A. C.								
A 9							-		
A 12							164		
A 14							93		
A 15							143		
126							183		
A 3							185		
A 6							208		
129							191		
A 18							134		
53							-		
107							374		
A 20							199		
A 21							180		
A 22							115		
A 23							175		
A 27							136		
A 35							259		
143							203		
148							175		
142	23.7	31.9	27.0	41.9	43.0	43.0	110/70	12	175
A 36	34.1	38.6	38.6	56.4	56.4	56.4		6 1/2	210

*All percentages represent decreases except those marked which represent increases

TABLE VA INITIAL BLOOD VOLUME DATA
Further Classification of Cases

Corrected "A"	Observed values minus all fluid received until blood volume determination was completed
Corrected "B"	Observed values minus all fluid received from time patient was evaluated (usually) upon arrival at hospital until blood volume determination was completed
All percentages represent decreases from calculated normal except those marked by asterisk which represent increases	

cept that if held at the bedside may do real harm in providing an excuse for limiting resuscitative effort. In short, if "irreversible shock" in the usual sense was present, we missed it. If toxins caused any of the shock we saw (excepting that due to clinically apparent, overwhelming bacterial infections) we failed to recognize it. The shock we saw was caused by blood loss (or loss of fractions of the blood). It was cured by blood administration.

The blood volume was determined by Gregersen's method (see the Appendix of the Monograph mentioned in the footnote, page 672 for the details of methods used) in 67 men* shortly after they arrived at the most forward hospital, in most cases a field hospital. In our studies the normal blood volume has been considered to be 85 per cent of the body weight (Gregersen). The blood volume found has been recorded. But this has also been corrected by subtraction of all plasma or blood administered (following the wounding and before the determination was made). This is recorded as "Series A" to distinguish it from the uncorrected volumes. Correction "B" data is the observed blood volume less only the volume of fluid administered during the period the determination was in progress. The figures reported in the tables represent the amount of blood lost expressed as per cent of the calculated normal blood volume (85 per cent of

TABLE VB NO SHOCK (12 CASES)

CASE NUMBER	BLOOD VOLUME CHANGE (% OF NORMAL)				BLOOD				NOTES AFTER WOUND	BLOOD SUGAR (MG %)
	OB SERVED	CORRECTED		OB SERVED	A		B	(MM HG)		
		'A'	B		A	B				
A 13	18.4	18.4	18.4	36.5	36.5	36.5	150/10	14 1/2	1.1	
A 4	8.2	8.2	8.2	31.1	31.1	31.1	132/72	4 1/2	93	
A 16	8.9	10.5	8.2	12.2	12.2	12.2	130/70	5 1/4	139	
131	7.8	11.3	7.8	3.9	3.9	3.9	120/76	15 1/4		
A 19	31.9	31.9	31.9	42.5	42.5	42.5	116/78	8 1/4	167	
A 20	2.8	2.8	2.8	11.5*	11.5*	11.5*	140/30	2 3/4	110	
A 23	17.0*	17.0*	17.0*	13.3*	13.3*	13.3*	128.40	4 1/2	127	
121	15.3*	2.8	2.8	14**	1.6	1.6	120/64	10 1/4		
91	26.0	37.7	37.7	43.1	42.9	37.9	109/78	9 1/4		
107	21.3	36.9	29.1	31.1	39.0	39.0	150/80	3 1/4		
A 24	0.3	10.3	10.3	4.1*	4.4	6.4	110/10	4 1/2	140	
A 39	7.1	7.1	7.1	20.5	20.5	20.5	124.72	4	144	

*All percentages represent decreases except those marked which represent increases
Case A 27 is omitted because of probable technical error

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TABLE VI. SEVERE SHOCK (16 CASES)

CASE NUMBER	SEX	BLOOD PRESSURE			BLOOD PRESSURE			HOURS AFTER WOUNDING	BLOOD LOSS (CC)
		BEFORE	AFTER	REMARKS	BEFORE	AFTER	REMARKS		
147								133	163
149								17½	113
139								9	
A 98	♀	92	90	92	337	337	337	measurable	
A 99	♀	92	54.9	37.1	54	63.6	63.6	80/38	5½
105	♂	21.3	33.0	90.1	41.9	57	57	70/38	23
A 31	♀	10.9	16.6	8.2	0	19.0	19.0	80/68	1
100	♀	34.4	5.0	49.0	4.9	53.4	53.4	60/39	4
A 39	♀	41.6	39.3	48.7	47.0	66.1	66.1	0	1
A 91	♀	46	71.0	54.8	6.6	83.8	83.8	68/40	4
109	♀	33.3	33.9	30.0	61.8	64.1	64.1	58/0	3½
93	♂	11	34.0	30.3	17.0*	26*	26*	0	14½
110	♂	3.0	3.6	37.6	4.7	47.4	4.4	0	3
100	♀	28.4	60.0	65.0	41.1	76.6	6.6	80/40	4½
130	♂	31.3	51.6	40.5	51.6	67.0	67.0	60/40	5
131	♀	29.9	43.6	39.0	40.1	54.3	54.3	41/40	5½
119								11½	216

*All percentages represent decreases except those marked which represent increases

TABLE VI. BLOOD PRESSURE AND BLOOD LOSS

CASE NUMBER	BLOOD PRESSURE AT TIME OF OPERATION (MM HG)	SEVERITY OF SHOCK	BLOOD LOSS (CC)	HOURS AFTER WOUNDING	LOSS OF BLOOD (% OF CALCULATED NORMAL)			LOSS OF TOTAL CIRCULATION (% OF TOTAL)	
					FOUND	CORRECTION		FOUND	CORRECTION
						A	B		
A 3	133/90	Mod sev	145	4	34*	9	9	84.6	83
A 98	110/70	Slight	196	4	74	74	74	11.6	73.1
A 4	130/0	0	93	4½	8.2	8.2	8.2	639.0	31.1
108	39.0	Severe	3	3½	35.5	39.9	30.0	341.9	64.1
A 9	114/60	Slight	1.0	4	9.3	9.3	9.3	9.0	9.6
A 33	90/50	Mod sev	1.5	5½	9.9	9.3	9.3	58.5	40.6
A 10	130/70	0	139	5½	8.9	10.5	8.2	60.8	1.9
113	94/59	Slight	149	3½	14.9	90.0	20.2	5.31	94.9
A 30	80/40	Mod sev	115	½	37.9	99.5	549.9	46.8	
A 7		Head injury	315	½	31.6	31.6	31.6	510.6	47.0
93	0	Severe		14½	11	31.0	30.3	1903.9	9.6
A 90	140/80	None	110	1½	9.8	9.8	9.8	1.00.6	11.3
A 13	150/0	None	1.1	19	18.4	18.4	18.4	3.9	39
A 18	30/0	Mod sev	134	8	4.8	4.8	4.8	394.4	61.1
114	90/60	Slight		1	8.8	6.7	1.5	4.8	30.6
A 30	86/66	Mod sev	1.9		37.5	41.9	37.5	41.9	37.5
A 8	108/70	Mild		1	14.8	14.8	14.8	6.4	93.3
143	80/54	Mod sev	0.3	6	3.1	13.9	18*	90.9	4.0
147	80/48	Severe	165	17½	6.5	94.1	14.3	94.1	4
A 90	90/50	Slight	145	13½	33.9	37.9	33.9	4.91	56.6
111	120/80	Slight	157	14½	7	7.1	7.1	8.19	5.1
140	100/60	Slight	141	4½	16.9*	1.1	1.1	100	5.9
A 99	80/38	Severe	38*	3½	9.2	34.9	37.1	40.0	63.6
A 37	120/88	Mod sev	136	3	41.6	50.4	50.4	41.6	6.4
A 40	100.64	Slight	196	3½	3.5	3.5*	3.5	939.4	5.5
106	100/60	Mod sev	183	2½	30.9	37.3	3.3	600.6	44.4
17	90/40	Mild		11	19.9	59.4	44*	331.2	63.9
A 98	64/20	Severe	918	6½	9	9	9	5.7	38
A 19	116/78	None	167	8½	31.9	31.9	31.9	5.93	47.5
A 39	104/70	None	194	4	7.1	7.1	1	96.4	95.5

*All percentages represent decreases except those marked which represent increases

Relationship of Blood Loss to Type of Wound

Fifty nine of the patients suffered primarily from a single major wound—abdomen, chest, or peripheral wound—and could be accurately classified (see Tables XI and XII, and Charts 7 and 8)

TABLE XII RELATIONSHIP BETWEEN HEMOGLOBIN LOSS AND TYPE OF WOUND
Figures Represent Hemoglobin Loss Expressed as Per Cent of the Calculated Normal Total Hemoglobin in the Circulation, All Values Before Operation and Anesthesia

TYPE OF WOUND	FOUND	CORRECTION "B"
Peripheral wounds (32 cases)	40.0 \pm 3.4	46.0 \pm 3.1
Abdominal wounds (13 cases)	17.3 \pm 6.0	24.0 \pm 6.1
Thoracic wounds (14 cases)	34.4 \pm 3.2	37.8 \pm 3.2
Thoracoabdominal wounds (6 cases)	20.3 \pm 6.5	23.6 \pm 6.3
Total (65 cases)	32.5 \pm 2.5	37.8 \pm 2.6

The huge standard errors present in several instances reflect the wide variation in the results found. At first glance the loss of blood volume appears to be greater in the peripheral wounds than it is in the abdominal, for example. This may be true, but the data are not extensive enough to show it, the true state of affairs possibly being masked by the small number of cases, the wide variability in blood loss from one case to another and the dilution of the blood volume postwounding by the movement of fluid from the tissues to the blood stream. A more revealing situation can probably be found in the hemoglobin loss. Here there is a significantly greater hemoglobin loss in men with peripheral wounds than in those with abdominal wounds. In this case, the facts are not obscured by hemodilution. This difference shown here fits in with the demonstration made previously that patients with compound fractures of long bones or traumatic amputations constitute a higher percentage in the severe shock group than do those with abdominal wounds. While the following data

TABLE XIII RELATIONSHIP BETWEEN BLOOD LOSS AND TYPE OF WOUND IN PATIENTS WHO HAD RECEIVED 0 TO 1 UNIT OF PLASMA BEFORE THE DETERMINATION
Figures Represent Blood Loss Expressed as Per Cent of the Calculated Normal, All Values Before Operation and Anesthesia

TYPE OF WOUND	LOSS OF BLOOD VOLUME (CORRECTION "A")	LOSS OF TOTAL HEMOGLOBIN (CORRECTION "B")
Peripheral wounds (18 cases)	23.9 \pm 3.9	38.0 \pm 4.3
All other wounds (22 cases)	15.3 \pm 3.9	22.5 \pm 3.8
Total (40 cases)	19.1 \pm 2.4	29.5 \pm 3.1

TABLE XIV EXTREMITY WOUNDS LOSS OF CIRCULATING BLOOD AND TOTAL CIRCULATING HEMOGLOBIN DETERMINED VALUES MINUS ALL BLOOD AND PLASMA REPLACEMENTS
Per Cent Lost From Calculated Normal

	NO FRACTURE	COMPOUND FRACTURE	TRAUMATIC AMPUTATION
Blood volume Loss A	19 \pm 8.1 (7 cases)	40.8 \pm 4.2 (19 cases)	37.0 \pm 3.2 (5 cases)
Hemoglobin Loss B	32.8 \pm 7.0 (7 cases)	51.6 \pm 4.2 (19 cases)	43.0 \pm 3.9 (5 cases)

*Correction A used on blood loss observed values less all fluid received until time blood volume determination was completed

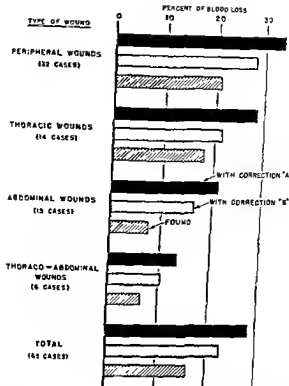


Chart 7—Relationship between blood loss and type of wound. Figures represent blood loss expressed as per cent of the calculated normal blood volume all values before operation and anesthesia.

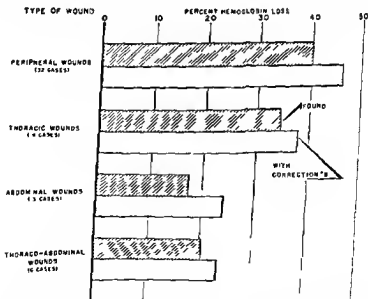


Chart 8—Relationship between hemoglobin loss and type of wound. Figures represent hemoglobin loss expressed as per cent of the calculated normal total hemoglobin in the circulation, all values before operation and anesthesia.

indicated in Tables XI and XII because the group includes fewer of the patients in severe shock. All tables show a greater average loss of hemoglobin than of blood volume. This is explained by hemodilution which normally takes place after blood loss. Red blood cells are not replaced appreciably during the interval from wounding to forward hospital arrival except by transfusion.

Time From Wounding to Blood Loss Measurement

There is no important increase in blood volume loss or in hemoglobin loss with the passage of time. A misinterpretation would probably be easy here. Quite probably those men who were suffering from continuing blood loss were whenever this was known given priority of evacuation and reached the hospital sooner than would otherwise have been the case (see Table XI and Chart 11). This was often supported by the somewhat greater blood loss found in those who arrived early against those who came in later.

TABLE XI BLOOD LOSS AND TIME AFTER WOUNDING

HOURS AFTER WOUNDING	CORRECTED* BLOOD LOSS A (% NORMAL)	CORRECTED HEMOGLOBIN LOSS B (% NORMAL)
0 to 6	29.0 (41 cases)	37.5 (41 cases)
7 to 12	31.9 (17 cases)	42.3 (17 cases)
13 and up	24.7 (9 cases)	35.8 (9 cases)

*Observed values less blood and plasma administered before blood determination was completed.

Relationship of Blood Loss to Degree of Shock

It is well known that individuals even healthy previously normal young soldiers do not respond alike to a given blood loss. This fact plus the inexactness inherent in any clinical appraisal not to go into the errors of the experimental method used—all of these things might have tended to obscure a real relationship here that they did not is clear from Table XVI, Charts 12 and 13. The greatest blood volume loss was found in two patients in moderate and severe shock. They had lost respectively 78.6 and 75.7 per cent of their normal blood volume (correction A). Patient A 21 who had extremity wounds and was in severe shock lost 83.8 per cent of the normal amount of his hemoglobin.

TABLE XVI BLOOD LOSS IN SHOCK

DEGREE OF SHOCK	BLOOD LOSS	HEMOGLOBIN (NORMAL)
None		+ 4.7 (cases)
Light		+ 4.0 (cases)
Moderate		+ 3.3 (cases)
Severe		+ 3.0 (cases)

*Blood and volume determined before blood

are few, they are pertinent to the present discussion and are presented for what they are worth (see Table XIV, and Chart 10)

The blood loss with compound fractures is greater than it is in traumatic amputation, probably due to the greater tissue damage usually found in the former case

Table XIII (Chart 9) shows the blood and hemoglobin losses in cases selected to include only those patients who had received no more than 0 to 1 unit of plasma before the determination. The losses here are smaller than those

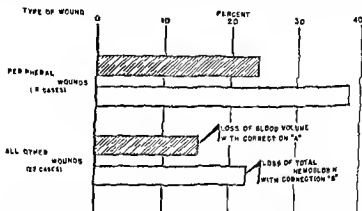
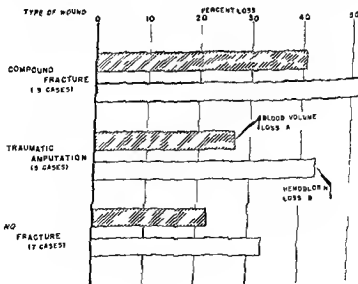


Chart 9.—Relationship between blood loss and type of wound in patients who had received only 0 to 1 unit of plasma before the determination. Figures represent blood loss expressed as per cent of the calculated normal. All values before operation and anesthesia.



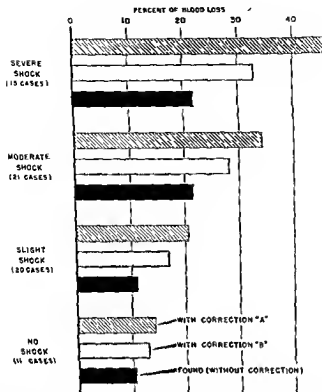


Chart 12—Blood loss in shock. Figures represent average loss expressed as per cent of the calculated normal blood volume determinations before operation or anesthesia.

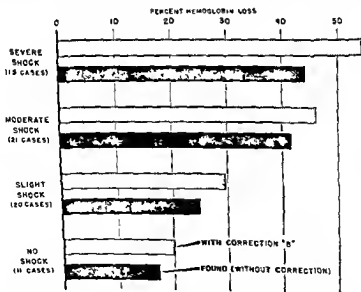


Chart 13—Relationship between loss of hemoglobin and degree of shock. Figures represent loss of hemoglobin expressed as per cent of calculated normal total circulating hemoglobin.

As a generalization one can say that when one third of the blood volume is lost, clinical shock of more than slight degree is present when one half is gone severe shock is present

In individual cases 60 to 75 per cent of the corrected blood volume or 60 to 75 per cent of the corrected total hemoglobin may be lost with survival See Cases A 17, A 21, A 29 A 37 A 38 127 and 139 for examples

Again speaking generally, on arrival at the hospital the percentage of hemoglobin loss is greater than the blood volume loss This is understandable in view of the well known mechanism for replenishing blood volume at the expense of tissue fluid Once the readily available reserves of hemoglobin (red cells) are called into action no mechanisms are available to cope immediately with the needs of the body, and greater falls in hemoglobin are apparent than is the case with the blood volume

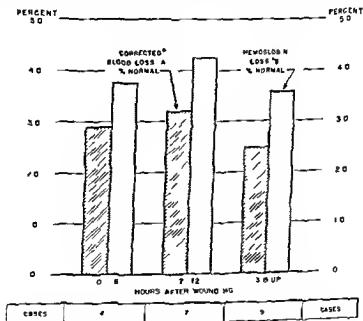
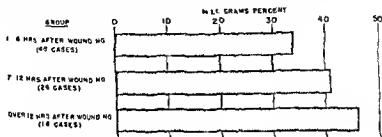


Chart 11.—Blood loss and the time after wounding (observed values less blood and plasma administered before blood determination was completed)

We have tried various schemes for handling our shock data some have attempted this by separating the effects of blood loss alone from those supposedly accounted for by sympathico-adrenal activity Practically this is impossible Moreover the validity of any such separation even if possible must be questioned Take the matter of increased glycogenolysis in shock How is one to deal with this? After all of the recent advances in knowledge of carbohydrate metabolism it seems to be too great a simplification to hang the explanation on the rather shaky pegs of sympathico-adrenal activity Therefore we take refuge in our purpose of preventing a source book in stating our findings and leaving to postwar leisure the search for full significance

Relationship to Delay in Hospital Arrival

With the passage of time following wounding, the nonprotein nitrogen blood level rises. This upward swing (Table XVII, Chart 14) of the nonprotein nitrogen blood level offers a basis for some interesting speculation, out of place here, but one can ask in passing, is this rise a reflection of decreased renal blood flow? Does this rise mean that renal impairment is initiated by the wound and continues, with accumulation of nonprotein nitrogenous products? Does this presumed malfunction set the stage for later trouble with the kidneys?



PERCENT DISTRIBUTION OF WOUNDS BY TYPE

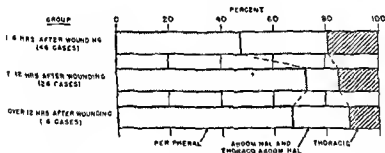


Chart 14

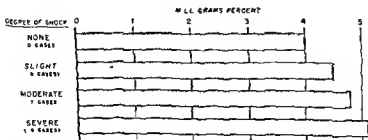


Chart 15—Admission uric acid levels divided according to clinical condition of patient.

The creatinine does not rise significantly with the passage of time preceding hospital entry neither do the uric acid, phosphorus, or magnesium (see Table XVIII). There is no correlation between the passage of time and the blood levels of chlorides sodium or carbon dioxide.

One great consequence of blood loss is the intense vasoconstriction the shrinkage of the capacity of the vascular bed to accommodate the decreased blood volume. Contraction of the spleen probably plays a relatively small role in compensating for the blood lost in battle. Other adjustments for blood loss take place, however. These are concerned with the entry of fluid into the blood vessels in a compensatory attempt. The greatest extravascular store of readily available fluid in the body is that in the extracellular space. Dehydration and oligemia may make quite early demands not only on this but also on the intracellular supply as well.

BIOCHEMICAL CHANGES ENCOUNTERED

(NITROGENOUS WASTE PRODUCTS, ELECTROLYTES, BILIRUBIN, BLOOD SUGAR)

The clinical appearance of the newly wounded man as well as his subsequent course, offers abundant evidence that profound changes have occurred in his internal state by the time he is admitted to a hospital. To be reported here are changes chiefly in the blood. (When the urine is the vehicle, this is stated.) These changes are significant not only as they reveal the extent of the problem at hand but also once known they offer some basis for reasonable therapy. Several factors influence the presence or extent of the abnormalities found.

Relationship to Location of Wound

No significant relationship between nonprotein nitrogen, creatinine, urea, acid phosphorus, magnesium, chlorides, sodium and carbon dioxide and the location of the wound has been found (for example see Table XVI A). The other data are equally "negative," and for brevity are omitted from this section.

TABLE XVI A BIOCHEMICAL DATA AMONG THE WOUNDED CLASSIFIED ACCORDING TO TYPE OF WOUND
All Determinations Done Before Operation and Anesthesia

WOUNDS	NON PROTEIN NITROGEN	CRE ATININE	N P N * CREATIN INE X 10	URIC ACID	PHOS PHORUS	MAG NESIUM
Peripheral wounds with out fracture	39.0 ± 3.7 (11 cases)	1.7 ± 0.16 (11 cases)	2.6 ± 0.2 (11 cases)	5.0 (5 cases)	4.0 ± 0.6 (6 cases)	2.3 (5 cases)
Peripheral wounds with fracture	41.0 ± 1.8 (32 cases)	1.6 ± 0.1 (31 cases)	2.7 ± 0.13 (31 cases)	4.4 ± 0.2 (19 cases)	4.9 ± 0.5 (24 cases)	2.3 ± 0.13 (20 cases)
Peripheral wounds with traumatic amputation	47.0 ± 4.3 (6 cases)	1.5 ± 0.3 (6 cases)	3.7 ± 0.6 (6 cases)	5.5 (2 cases)	4.9 (4 cases)	2.0 (3 cases)
Abdominal wounds† (all cases)	34.0 ± 2.2 (19 cases)	1.4 ± 0.12 (19 cases)	2.7 ± 0.12 (19 cases)	4.9 ± 0.29 (16 cases)	3.9 ± 0.3 (17 cases)	2.0 ± 0.1 (16 cases)
Patients with kidney in jury	35.0 ± 2.9 (9 cases)	1.5 ± 0.2 (9 cases)	2.6 ± 0.29 (9 cases)	6.0 ± 0.99 (6 cases)	4.0 ± 0.5 (9 cases)	2.0 ± 0.12 (7 cases)
Patients with liver in jury	37.0 ± 3.0 (10 cases)	1.3 ± 0.10 (10 cases)	3.0 ± 0.21 (10 cases)	5.8 ± 0.93 (6 cases)	3.9 ± 0.4 (9 cases)	2.0 ± 0.1 (6 cases)
Thoracoabdominal wounds*	38.0 ± 3.1 (7 cases)	1.5 ± 0.09 (7 cases)	3.0 ± 0.37 (7 cases)	6.1 (5 cases)	4.5 ± 0.55 (7 cases)	2.0 (5 cases)
Thoracic wounds	36.0 ± 2.5 (14 cases)	1.3 ± 0.15 (14 cases)	2.9 ± 0.6 (14 cases)	4.1 ± 0.63 (9 cases)	4.2 ± 0.28 (13 cases)	1.9 ± 0.10 (11 cases)

* N P N represents nonprotein nitrogen
† With and without kidney and liver injury

Relationship to Clinical Condition (Degree of Shock)

The interesting relationships of nonprotein nitrogen, creatinine phosphorus, and magnesium to clinical condition are shown in Table XIX. Statistically significant rises are present for nonprotein nitrogen, phosphorus, creatinine and magnesium as one progresses from "No Shock" to "Severe Shock," with the chief difference occurring between the moderate and severe shock groups in most cases. Uric acid, at first glance appears to rise significantly, but examination of the data fails to reveal a truly significant effect (see Table XIX, Chart 15). While a real rise might be demonstrated if more data were available it is not shown here. As might be expected, the same positive correlation is present for nonprotein nitrogen, creatinine phosphorus, and magnesium, as

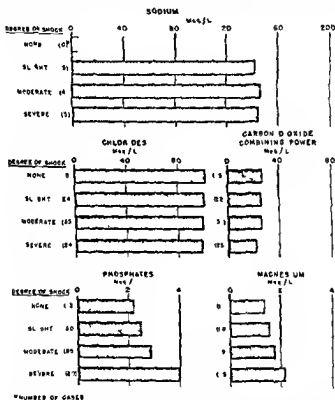


Chart 16—Average plasma electrolytes on admission no crush cases

shown previously when these substances are plotted against blood loss expressed in five increasing categories from 0 to 40 per cent loss and over with this approach uric acid failed again to show a significant rise (see Table XX). As shown before there is no correlation between passage of time and the degree of shock encountered in that the elapsed time was the same in each of the four groups No Shock Slight Moderate and Severe Shock. This does not say that continuing hemorrhage for example is not related to degree of shock, certainly it is. The important factor in the development of shock is the character of the wound especially hemorrhage not the passage of time per se.

TABLE XVII RELATIONSHIP OF NONPROTEIN NITROGEN BLOOD LEVEL TO THE PASSAGE OF TIME
Values Before Operation and Anesthesia

HOURS AFTER WOUNDING	NONPROTEIN NITROGEN (MG %)	DISTRIBUTION OF WOUNDS IN THESE CASES
1 to 6	31.2 ± 1.1 (48 cases)	48% Peripheral 33% Abdominal and thoracoabdominal 19% Thoracic
7 to 12	41.2 ± 1.7 (26 cases)	73% Peripheral 12% Abdominal and thoracoabdominal 15% Thoracic
13 and up	46.3 ± 3.0 (18 cases)	67% Peripheral 22% Abdominal 11% Thoracic

TABLE XVIII THE PASSAGE OF TIME AND SEVERAL BLOOD CONSTITUENTS
Values Before Operation and Anesthesia

HOURS AFTER WOUNDING	CREATININE (MG %)	URIC ACID (MG %)	PHOSPHORUS (MG %)	MAGNESIUM (MG %)
1 to 6	1.3 ± 0.1 (50 cases)	4.5 ± 0.4 (38 cases)	4.1 ± 0.3 (49 cases)	2.1 ± 0.1 (41 cases)
7 to 12	1.6 ± 0.1 (26 cases)	4.7 ± 0.5 (15 cases)	4.8 ± 0.3 (19 cases)	2.1 ± 0.1 (15 cases)
13 to 24	1.7 ± 0.2 (10 cases)	5.9 ± 0.7 (7 cases)	4.2 ± 0.5 (11 cases)	1.8 ± 0.1 (9 cases)

TABLE XIX BIOCHEMICAL DATA AMONG WOUNDED IN DIFFERENT DEGREES OF SHOCK
All Determinations Made Before Operation and Anesthesia

DEGREE OF	CREATININE	PHOS	MAGNESIUM
1		3.3 ± 0.24 (14 cases)	1.7 ± 0.05 (11 cases)
2		3.8 ± 0.18 (20 cases)	1.9 ± 0.06 (17 cases)
3		4.3 ± 0.23 (21 cases)	2.0 ± 0.09 (20 cases)
4		5.8 ± 0.52 (21 cases)	2.5 ± 0.16 (16 cases)

TABLE XX BIOCHEMICAL DATA AMONG THE WOUNDED, CLASSIFIED ACCORDING TO AMOUNT OF BLOOD LOST EXPRESSED AS PER CENT OF THE NORMAL BLOOD VOLUME
(CORRECTION "A" APPLIED)

All Values Before Operation and Anesthesia

LOSS OF BLOOD VOLUME	CREATININE	PHOS	MAGNESIUM
1			1.8 ± 0.07 (8 cases)
2			1.9 ± 0.07 (9 cases)
3			1.8 ± 0.05 (11 cases)
4			2.1 ± 0.1 (17 cases)
5			2.4 ± 0.14 (15 cases)

TABLE XXIIA PLASMA LACTIC ACID CONCENTRATION IN THE WOUNDED

SOURCE	LACTIC ACID CONCENTRATION IN PLASMA (IN MILLIGRAMS PER CENT)		
	MINIMUM	MAXIMUM	AVERAGE
Normal controls (7 active soldiers)	17	24	21
Wounded examined 6 to 19 hr after wounding (average 10 hr) (5 cases)	29	46	38
Patients in third to fifth week of convalescence from war wounds (10 cases)	14	21	16

Urinary pH and specific gravity indicate that these men had essentially normal renal function at the time they were wounded, in that they could make both an acid and a concentrated urine.

For a further discussion of the acid base relationship, see the section on Kidney Function.

Creatinuria

The appearance of creatine in the urine of adult males is abnormal. On the assumption that there might be some abnormality in the metabolism of creatine and creatinine in shock, the urine was examined for creatine in 32 soldiers shortly after wounding and at other times after operation. The results are

TABLE XXIIIB CREATINURIA

CASE NUMBER	SPECIMENS EXAMINED PREOPERATIVELY		SPECIMENS EXAMINED POSTOPERATIVELY		DEGREE OF SHOCK	LIVED OR DIED	COMMENT
	FOUND POSITIVE	FOUND NEGATIVE	FOUND POSITIVE	FOUND NEGATIVE			
112				1	Severe	Lived	Azotemia
A 3				1	Mod sev	Lived	
83		1	1		Severe	Lived	
A 4	1				None	Lived	'Anuria'
108		1	3		Severe	Died	
A 2		1		1	Slight	Lived	
109				2	None	Lived	NPN to 63
A 16		1			None	Lived	
113	1		1		Slight	Lived	
120			1		Slight	Died	'Anuria'
111		1	4		Slight	Lived	
A 40			1		Slight	Lived	
126		1	1		Mod sev	Died	Oliguria
127				1	Slight	Lived	
110			3		Severe	Lived	
131		1	2	1	Severe	Died	Oliguria
124		1			None	Lived	
118			2		Severe	Died	
130	2		1	1	Severe	Lived	Azotemia
101			3		Mod sev	Lived	
129	1			1	Mod sev	Died	
A 5	1		1		Slight	Lived	Anuria
117			1	1	Mod sev	Died	
A 6	1		1		Mod sev	Lived	
125			1	1	Severe	Lived	NPN to 60
A 1		1	1		Slight	Lived	
102			6		None	Died	
133				2	Severe	Lived	Oliguria
106				2	None	Lived	
121				1	Severe	Died	
107			1		Mod sev	Died	Oliguria
123			2		Severe	Died	
Totals	7	9	37	16			

Information relevant to acid base balance is shown in the Tables on Electrolytes and Urine (Tables XXI and XXII, see Chart 16). An acidosis was present in those patients with severe shock and is reflected in the carbon dioxide combining power. A significant fall of carbon dioxide combining power can be correlated with shock. Evidence that these low values are due to a metabolic acidosis is presented in the chapter on azotemia in the Monograph mentioned in the footnote, page 672. Plasma chlorides were uniformly normal in all groups of cases, likewise, urinary chlorides, although they showed wide variations in concentration, were essentially normal. There is then no evidence of salt deprivation at this stage, that is, on hospital entry. Phosphates, although significantly higher in the severe shock than no shock group, in terms of total anions, could have had little effect on the acid base balance. Plasma proteins are not included in Table XXI, but they showed insufficient variation in terms of electrolyte concentration to have affected acid base balance.

TABLE XXI AVERAGE PLASMA ELECTROLYTES ON ADMISSION
No Crush Cases

	ALL CASES	NO SHOCK	SLIGHT SHOCK	MODERATE SHOCK	SEVERE SHOCK
Carbon dioxide combining power (Meq/L.)	20.3 ± 0.5 (93 cases)	27.9 ± 1.0 (15 cases)	26.1 ± 0.7 (22 cases)	28.1 ± 0.4 (31 cases)	1.1 ± 0.9 (9 cases)
Chlorides (Meq/L.)	100.5 ± 0.6 (96 cases)	102.0 ± 3.0 (15 cases)	101.0 ± 0.7 (24 cases)	100.0 ± 0.5 (33 cases)	99.5 ± 0.9 (24 cases)
Phosphates (Meq/L.)	3.0 ± 0.2 (78 cases)	2.2 ± 0.3 (13 cases)	2.5 ± 0.2 (20 cases)	2.9 ± 0.3 (31 cases)	4.0 ± 0.3 (9 cases)
Magnesium (Meq/L.)	1.8 ± 0.07 (64 cases)	1.4 ± 0.05 (11 cases)	1.6 ± 0.08 (18 cases)	1.8 ± 0.10 (19 cases)	2.2 ± 0.16 (16 cases)
Albumin (Gm/l serum) (Meq/L.)	144.3 (13 cases)	—	144.1 (6 cases)	147.1 (4 cases)	144.7 (5 cases)

TABLE XXII AVERAGE PREOPERATIVE URINES FROM TWENTY SIX CASES
Specific Gravity of Urine 1.027 ± 0.001 (Twenty six Cases)

	ALL CASES	NO SHOCK	SLIGHT SHOCK	MODERATE SHOCK	SEVERE SHOCK
pH	5.9 ± 0.1 (26 cases)	6.3 ± 0.1 (7 cases)	5.7 ± 0.1 (6 cases)	5.7 ± 0.1 (6 cases)	5.7 ± 0.2 (7 cases)
Chlorides mg % as NaCl	819 ± 10.3 (23 cases)	1128 ± 18.3 (2 cases)	915 ± 17.9 (8 cases)	423 ± 19.3 (5 cases)	704 ± 24.1 (5 cases)
Grams sodium* received since wounding	2.2 (20 cases)	1.0 (4 cases)	0.8 (5 cases)	3.7 (4 cases)	3.1 (7 cases)
No sodium since wounding	7 cases	3 cases	3 cases	2 cases	0 cases

*10 Gm. of Sodium citrate furnish 5 Gm. of Sodium
10 Gm. of Soda bicarbonate furnish 2.7 Gm. of Sodium

The blood was examined for lactic acid in five patients shortly after wounding. The findings were compared with those from tests done in normal active soldiers and in bed patients convalescing from severe wounds. The results are recorded in Table XXIIA. They show a twofold increase in the concentration of lactic acid in the wounded when compared with normal active soldiers and with patients at bed rest.

Sodium was measured in too few cases for reliable averages. Most of the values found were within the normal range. Magnesium like phosphates on the acid side was increased, but not sufficiently to affect total acid base equilibrium.

Creatinuria was present at some time in all but one of the patients who died and in whom the tests were made (Table XXIII). It was present in approximately one half the patients who lived. Table XXIII suggests that creatinuria is more likely to occur in the group of patients who had been in severe shock than in the others. Of the 18 patients who had been in moderately severe to severe shock, only 4 failed to show creatinuria. It appears that creatinuria may be the result of metabolic changes which accompany shock.

Van den Bergh and Plasma Hemoglobin Levels

Type of Wound—On comparison of the type of wound with bilirubin and plasma hemoglobin, no impressive relationships are found (see Table XXIII).

The Passage of Time—The van den Bergh index rises significantly with increasing time from wounding to examination (see Table XXIV). This may be due to the absorption of breakdown products from hematomas, and to impaired liver function (see the following section on Liver Function in the Newly Wounded Man). The situation is simpler here (since these patients have in most cases not yet been transfused with blood) than it is later when large volumes of blood have been given. These may tend to elevate the bilirubin level. The plasma hemoglobin level appears to rise with the passage of time, but this is not significant, as far as the data at hand are concerned.

TABLE XXIV VAN DEN BERGH AND PLASMA HEMOGLOBIN LEVELS COMPARED WITH THE PASSAGE OF TIME

HOURS FROM WOUNDING UNTIL BLOOD SAMPLE DRAWN	VAN DEN BERGH (MG % OF BILIRUBIN)	PLASMA HEMOGLOBIN (MG %)
1 to 6	0.45 ± 0.05 (47 cases)	11.4 ± 0.9 (48 cases)
7 to 12	0.64 ± 0.07 (23 cases)	9.4 ± 1.4 (27 cases)
13 to 24	0.69 ± 0.07 (13 cases)	11.1 ± 2.1 (15 cases)

Clinical Condition (Degree of Shock)—There is no clear relationship of shock to bilirubin or to plasma hemoglobin levels (Table XXV). However, when the bilirubin level is placed against the blood loss (Correction "A") a significant relationship seems to emerge, although the values are all at a rather low level (Table XXVI). Presumably the rise is to be accounted for by hemolysis.

TABLE XXV VAN DEN BERGH AND PLASMA HEMOGLOBIN LEVELS COMPARED WITH DEGREE OF SHOCK

All Values Before Operation and Anesthesia. Excluding Crush Cases

DEGREE OF SHOCK	VAN DEN BERGH (MG % OF BILIRUBIN)	PLASMA HEMOGLOBIN (MG %)
None	0.43 ± 0.08 (11 cases)	12.1 ± 1.8 (14 cases)
Slight	0.69 ± 0.10 (23 cases)	11.3 ± 1.6 (23 cases)
Moderate	0.54 ± 0.06 (27 cases)	10.9 ± 1.4 (33 cases)
Severe	0.47 ± 0.05 (21 cases)	8.8 ± 0.9 (24 cases)

presented in Tables XXIB and XXIC Sixty nine urine specimens were tested (see Table XXID) Creatine was found in the urines of 22 of the 32 patients (Tables XXIC and XXID) Nearly one half the cases (6 out of 10) showed creatine in the urine when examined preoperatively, while 20 of 28 patients whose urines were examined postoperatively were positive for creatine

TABLE XXIC ANALYSIS OF RESULTS IN THIRTY TWO PATIENTS TESTED FOR CREATINEMIA

CLASSIFICATION	DEGREE OF SHOCK		RELATION TO OPERATION*			LIVED (NUMBER OF CASES)	DIED (NUMBER OF CASES)
	NONE TO SLIGHT (NUMBER OF CASES)	MODERATE TO SEVERE (NUMBER OF CASES)	PREOPERATIVE (NUMBER OF CASES)	POSTOPERATIVE (NUMBER OF CASES)	BOTH (NUMBER OF CASES)		
Patients who had both positive and negative urinalyses (9 cases)	2	7	Pos Neg	2 5	8 5	4	5
Patients who had only negative urinalyses (10 cases)	6	4	2	6	2	9	1
Patients who had only positive urinalyses (13 cases)	6	7	1	9	3	8	5
Total 32 cases							

*Four cases had a negative as well as a positive postoperative value and are therefore counted twice here. Two cases had no preoperative determination. Only one case was negative postoperatively and positive preoperatively.

TABLE XXIID SUMMARY OF SIXTY NINE URINE SPECIMENS WHICH WERE TESTED FOR CREATININE

SOURCE	POSITIVE (44 SPECIMENS)	NEGATIVE (25 SPECIMENS)
Preoperative	7	9
Postoperative	37	16
From patients who were in none or slight degrees of shock	18	11
From patients in moderate or severe shock	26	14
From patients who died subsequently	20	7
From patients who lived subsequently	24	18

TABLE XXIII VAN DEN BERGH AND PLASMA HEMOGLOBIN LEVELS IN PATIENTS WITH VARIOUS KINDS OF WOUNDS

TYPE OF WOUND	VAN DEN BERGH (MG % OF BILIRUBIN)	PLASMA HEMOGLOBIN (MG %)
Liver	0.36 ± 0.01 (9 cases)	10.7 ± 1.4 (10 cases)
Kidney	0.42 ± 0.07 (8 cases)	17.4 ± 0.3 (9 cases)
Intraabdominal	0.43 ± 0.11 (15 cases)	10.1 ± 1.8 (16 cases)
Thoracoabdominal	0.39 ± 0.04 (7 cases)	10.7 ± 2.2 (7 cases)
Thoracic	0.54 ± 0.07 (15 cases)	10.1 ± 1.6 (15 cases)
Soft parts with fracture	0.57 ± 0.05 (36 cases)	10.9 ± 1.1 (42 cases)
Soft parts without fracture	0.49 ± 0.12 (6 cases)	11.3 ± 2.9 (10 cases)

TABLE XXVI BILIRUBIN AND PLASMA HEMOGLOBIN COMPARED WITH BLOOD LOSS
Three Cases With Slight Blood Volume Gain Considered to Have 0 Per Cent Blood Loss,
Crush Cases Excluded

BLOOD LOSS ^a CORRECTION "A"	0.5%	5.15%	15.25%	25.40%	OVER 40%
Bilirubin (mg %)	0.31 ± 0.07 (6 cases)	0.56 ± 0.10 (8 cases)	0.50 ± 0.10 (10 cases)	0.52 ± 0.05 (20 cases)	0.64 ± 0.11 (18 cases)
Plasma hemoglobin (mg %)	13.5 ± 2.6 (7 cases)	11.2 ± 3.6 (8 cases)	9.8 ± 2.0 (11 cases)	14.3 ± 1.6 (20 cases)	10.0 ± 1.2 (18 cases)

^aObserved values less all fluid received until blood volume determination was completed

LIVER FUNCTION IN THE NEWLY WOUNDED MAN

As described in the section of the monograph mentioned in the footnote, page 672, on "Liver Function in the Severely Wounded," the only direct laboratory test of liver function carried out here was bromsulfalein excretion. The van den Bergh index and uric acid levels have also been considered as being in part at least related to liver function.

Bromsulfalein Retention

On Arrival at the Most Forward Hospital—In 59 patients the bromsulfalein retention on arrival was 12.4 ± 1.2 per cent, forty five minutes after 5 mg per kilogram body weight had been injected. This is well above the normal of 1.0 ± 0.1 per cent (see the Monograph, 45 subjects) and above our arbitrarily chosen upper limit of normal of 3 per cent.

Location of Wound—In 22 patients with extremity wounds there was 13.3 ± 2.3 per cent retention, and in 18 with abdominal wounds there was 14.7 ± 2.1 per cent retention—no difference. However, 11 men with penetrating chest wounds had only 7.0 ± 1.8 per cent retention, significantly lower than found in the other groups.

Relationship to Time Following Wounding—There was no difference in the bromsulfalein retention in men examined within the first six hours after wounding 14.4 ± 1.8 per cent (29 patients) or after the first six hours, 13.1 ± 1.6 per cent (19 patients).

Relationship to Shock—In 55 patients separated into the four groups, No Shock, Slight, Moderate and Severe Shock, no significant correlation with the bromsulfalein excretion could be found. Neither was there any correlation with blood volume or hemoglobin loss.

TABLE XXVII PLASMA GLUCOSE LEVELS (MG PER CENT)

	NONE	SLIGHT	MODERATE	SEVERE	
Relationship to degree of shock	134 ± 9 (9 cases)	149 ± 9 (14 cases)	178 ± 13 (19 cases)	202 ± 26 (13 cases)	
	0 TO 6 HR.	7 TO 12 HR.		13 TO 24 HR.	
Relationship to time after wounding	182 ± 13 (26 cases)	161 ± 10 (13 cases)		144 ± 7 (8 cases)	
	0 TO 5%	5 TO 15%	15 TO 25%	25 TO 40%	40% & UP
Relationship to blood loss (correction "A")	143 ± 12 (6 cases)	159 ± 15 (7 cases)	153 ± 7 (9 cases)	177 ± 18 (17 cases)	194 ± 23 (15 cases)

of blood in damaged tissues followed by absorption into the blood stream. There is no apparent correlation of blood loss with plasma hemoglobin values.

Blood Sugar

The blood sugar level* in the 56 wounded men we studied as they arrived at the forward hospital is above normal (Table XXVII and Chart 17). Some of the men had had plasma, but more had had a significant quantity of blood in resuscitation before the determination was made.

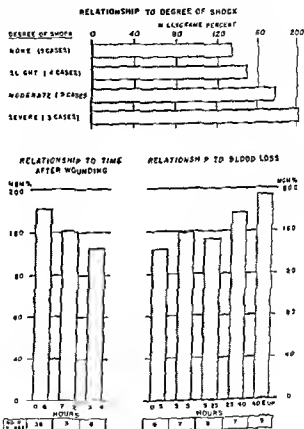


Chart 17—Plasma glucose levels

The blood sugar level appears to rise significantly both with increase in blood loss and with increase in severity of shock. The glucose level may fall with the passage of time following wounding but our data are not extensive enough to demonstrate this. Presumably the elevation in blood sugar level is due to mobilization of liver glycogen following adrenal activity and probably reflects the emotional and physical stress the individual has experienced.

*Normal by the method we used is 80 to 99 mg. per cent.

volume loss or hemoglobin loss and the degree of shock met clinically. This supports the view that the major cause of the shock we encountered is hemorrhage.

No important differences in blood volume or hemoglobin loss were encountered with the passage of time from wounding to examination. This is possibly to be accounted for by the high priority and consequent rapid evacuation given to bleeding wounds.

The clinical condition of the newly wounded man offers abundant evidence that his internal state has been profoundly altered by the time he enters the forward hospital. In addition to the matters already mentioned, this has been studied in terms of nitrogenous waste products, electrolytes, bilirubin, and blood sugar. In general, these were not found to be influenced by the location of the wound. The nonprotein nitrogen blood level rises rather strikingly with delay following wounding. The full significance of this is not clear, but it offers grounds for some interesting speculation. As one examines the four shock groups in sequence from no shock to severe shock, significant rises in nonprotein nitrogen, creatinine, phosphorus, and magnesium are found.

Acidosis was present in the patients with severe shock. There is a considerable fall in carbon dioxide combining power here as compared with that present in the no shock group of patients. The acidosis appears to be of the "metabolic" type.

No evidence of salt deprivation was found on hospital entry. Examination of the admission urine specimen with regard to hydrogen ion concentration and specific gravity indicates that the men studied had essentially normal renal function at the time they were wounded.

The van den Bergh index rises significantly with increasing time from wounding to examination. This is discussed briefly. No clear relationship of shock to bilirubin or plasma hemoglobin levels was found. The blood sugar level was found to be above normal. It is particularly high in the severe shock group.

Definite depression of liver function as measured by bromsulfalein retention was found on hospital arrival. This is discussed in its relationship to location of wound to time following wounding and to shock. The administration of one or two units of plasma appeared to impair liver function still further. This is a transitory effect and is not increased by giving three or four units of plasma.

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Relationship to Plasma Administration—Curiously enough, there was a great increase in bromsulfalein retention (140 ± 20 per cent, 25 patients) in men who had had one or two units of plasma over those who had had none (80 ± 20 per cent, 15 patients). Three or more plasma units did not increase the effect beyond that produced by one or two units. The effect was transient and disappeared between the first and second day following operation.

Van den Bergh and Uric Acid

Van den Bergh and uric acid have been discussed elsewhere in this same section.

SUMMARY

In the past, battle wounds have been described chiefly in terms of organic damage or tissue loss. The purpose of this section is to describe, shortly after the soldier has arrived at the forward hospital, the latent consequences of his wounds, as they have influenced organic function and produced abnormalities of the blood volume and chemistry, and abnormalities in the urine. These matters were studied before resuscitative efforts had yet been made, in 108 patients. Altogether, 186 patients were studied in the course of the work carried out by the Board for the Study of the Severely Wounded.

In considering patients who had received not more than one unit of plasma or none at all, it was observed that the hematocrit was higher in those with abdominal wounds than it was when the wounds were in the periphery of the body, but even in the case of abdominal wounds, the average hematocrits were somewhat below normal. While severe hemoconcentration can occur in burns in crush cases, and in abdominal wounds, this was infrequent in our cases and is by no means a general characteristic of shock as we saw it.

When the group of patients who had received little or no plasma or blood therapy at the time of first examination was divided into two parts, depending upon whether or not more or less than 30 per cent of the blood volume had been lost, a puzzling situation was apparent. The plasma protein concentration in the more severely bled-out group was 6.1 Gm per cent. This is 6.1 per cent below normal. On the other hand, the hematocrit in this same group had fallen to 36 from the normal of 47, a reduction of 23.4 per cent. The hematocrit thus fell about four times as much as the plasma proteins. One implication of this is that the blood had been diluted with protein rich fluid. Its possible source is discussed.

Evidence is presented that the plasma protein level was not influenced by the plasma therapy, although the hematocrit was. There is a sharp fall in hematocrit as one passes from the no-shock to the severe shock groups. Other examples of the independent variation of these two factors are given.

Men can lose about 75 per cent of their blood volume (corrected) and a corresponding quantity of hemoglobin and yet recover, more than previously generally supposed. The blood loss with various types of wounds is discussed. Data are given to show that there is a quantitative relationship between blood

no reaction. Polythene cellophane, on the other hand, causes a marked fibrous reaction and has been used in the treatment of aneurysms of the thoracic aorta, its branches, and of the pulmonary artery. The group which was reported included fourteen syphilitic aneurysms, two dissecting aneurysms, two congenital aneurysms and one of the pulmonary artery (Eisenmenger complex). The use of x rays was urged, particularly the lateral projection, and angiocardigraphy for diagnosis. Seventy five per cent of the aneurysms showed no pulsation. Many of the aneurysms were multiple. Congenital aneurysms simulated the embryonic aorta. Contact of the aneurysm with any bony structure is a contraindication to operation. Should the aneurysm compress the bronchus as evidence by atelectasis or apparent contact of aneurysm and bronchus, the chest should be decompressed prior to intubation by removal of a segment of clavicle, or excision of the upper two ribs unilaterally with the contiguous portion of the sternum or the resection of a V shaped wedge from the upper sternal margin. Preliminary decompression is usually indicated in aneurysms of the ascending aorta and innominate artery. The cellophane is applied loosely and fixed with sutures to prevent displacement. Even partial encirclement of the aneurysm with cellophane may produce relief. Polythene cellophane should not be applied to the aortic because it is too irritating. Dr. Karl Poppe reported his experience with twelve thoracic aneurysms of which only two were operable. Old age and cardiac decompensation are contraindications to operation. His best results were in fusiform aneurysms of the descending aorta. After operation the aneurysm does not decrease in size roentgenologically.

Arteriovenous Fistula of the Lung, Herbert C. Maier, New York—Arteriovenous fistula of the lung is in reality a cavernous hemangioma with an aneurysmal communication between the pulmonary artery and pulmonary vein, producing an inadequacy of oxygenation. Rarely the bronchial artery may communicate with the pulmonary vein. These fistulas are not of traumatic origin. They are frequently associated with telangiectasia about the face, especially the lips. A loud murmur is usually heard over the portion of the lung containing the fistula, this murmur is louder during inspiration. These patients present a picture of cyanosis, dyspnea, clubbing of the fingers and toes, and polycythemia with headache. The heart is not enlarged. Roentgenograms show a fluctuating tumor and the contour of the involved vessels. The red blood cell count may be as high as 10 per cent. The hematocrit may be up to 80 per cent. Arteriovenous fistulas of the lung should be distinguished from true polycythemia and congestive heart lesions. Malignant hemangioma of the lung is very rare and does not present the symptomatology of arteriovenous fistula. Treatment consists of excision of the fistulous communication, preferably by segmental resection. In practice, usually lobectomy or pneumonectomy is needed to eradicate the shunt. Adequate vascular channels must be preserved for the return of venous blood to the heart. Pneumothorax is wholly ineffective since it does not collapse the vessels involved.

ARTERIOVENOUS ANEURYSMS
SYSTEMIC CIRCULATION

PULMONARY CIRCULATION

Blood volume	Increased	Increased
Plasma volume	Increased	Normal
Hematocrit	Normal	Increased
Oxygen saturation	Normal	Decreased
Cardiac output	Increased	Normal
Enlargement of heart	Present	None

In the discussion Dr. R. H. Sweet reported two such cases in which the lesion was located in the right middle lobe. (This was similar to the case reported by Dr. John C. Jones at the Chicago meeting in 1933.) Dr. L. M. Shefts emphasized the familial character of these fistulas and said that phlebotomy should not be an uncommon complication because of the increase in blood viscosity. Dr. E. H. Byron said that disappearance of the polycythemia and cyanosis may be delayed after operation. Dr. Dewey Bigard said that these arteriovenous fistulas had undoubtedly been missed in the past. Dr. E. I. Evans, in speaking of the increased blood volume, wondered what became of the red blood cells and surmised that perhaps more blood was lost at operation than suspected. He pointed

Review of Recent Meetings

TWENTY SEVENTH MEETING OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

St. Louis, Mo., May 28-30, 1947

FREDERICK C. FISHBACK, M.D., WASHINGTON, D. C.

Dorsal Sympathetic Ganglionectomy for Intractable Asthma. Duane Carr, Memphis—Asthma, a syndrome of unknown origin, lacks a clear-cut physiologic pathology. The normal power to expand and contract is lost, and the bronchi remain constantly in contraction. The asthmatic state is probably a combination of swollen bronchial mucous membranes and an inability to cope with thick, viscid secretions, that it is due to bronchospasm is incorrect. Vagal stimulation does not produce asthma. Contraction of the bronchi persists between attacks. The bronchi may be more sensitive to adrenalin after denervation. Earlier workers had obtained varying degrees of relief by alcohol injections of the dorsal ganglia, by excision of the posterior pulmonary plexus, and by combination of dorsal ganglionectomy with excision of the pulmonary plexus. Surgery is restricted to asthmatic patients of long standing who are unresponsive to the usual drugs (namely, epinephrine or aminophyllin) and allergic procedures. Dr. Carr reported the end results of five cases in which operation was done three to ten years previously. The first two cases were by the Adson technique with excision of the third and fourth ganglia, the other three were performed through a periscapular incision, with removal of short segments of the third and fourth ribs, and extrapleural excision of the second, third, and fourth ganglia. Three of the patients were colored and two were white, all exhibited long periods of previous disability. Some were immediately relieved, in some relief was delayed, and one was worse immediately after operation, with later improvement. The severity and frequency of attacks have been markedly reduced so that they are controlled with aspirin or tetral. The patients are all able to work.

Dr. A. J. Grace described eleven cases in which he had excised the posterior pulmonary plexus, with three cures and varying degrees of benefit to the others. He emphasized the need for eradicating infection and eliminating allergies. Paravertebral block had not been effective in his hands. Surgical division of the vagal branches should reduce spasm and secretion, and benefit the accompanying emphysema. Dr. Osler Abbott also advocated the transpleural resection of the vagal components and noted that there were five fairly regular branches. Expiratory function is improved and vital capacity increases. Emphysema is benefited. He transplants the vagal stump into the pleura to discourage regeneration. Dr. Ralph Adams wondered whether any of these patients developed Raynaud's disease in the hands. He observed that since these were postganglionic operations it was reasonable to expect that the benefit would be delayed. He reported four cases of emphysema and cysts, in which two of the operations were of the vagal type and two were dorsal ganglionectomies. Dr. J. H. Chandler (the co-author) said that no instances of Raynaud's disease had occurred that the operation had no effect on bronchial inflammation or infection, and that they carefully avoided the stellate ganglion. Dr. Carr said that the recommended extrapleural procedure was designed to minimize shock in the debilitated patient.

Experiences With a New Method for the Control of Intrathoracic Aneurysms. Osler Abbott, Atlanta.—Although many methods have been used to obliterate aneurysms within the thorax, there has been continued search for a more satisfactory method. The goal has been the chronic progressive fibrous obliteration of the sac. Pearce has demonstrated the gradual occlusion of the dog's aorta with cellophane. Conflicting reports have resulted from the use of different types of cellophane. Moisture-resistant cellophane is nonirritating and causes

ment of esophageal cancer surgery has been the adaptation of the stomach, replacing the excised esophageal segment, within the chest. Continuity is reestablished by anastomosis of the mobilized stomach to the remaining esophagus. In effecting anastomoses in high lying cancers, the esophageal stump is brought over and anterior to the arch of the aorta. This technically difficult procedure carries with it an operative mortality three to five times as great as when the esophagus is left in place. From the standpoint of surgical anatomy, he urged that the esophageal tube be divided into fourths rather than the usual thirds. Exploration was done in sixty-seven cases and forty-four were operable. In age, the patients ranged from 52 to 84 years, but the general condition of the patient was more important than the chronologic age. All cases are biopsied preoperatively, and bronchoscopy is carried out as well as esophagoscopy, to exclude invasion of the bronchial tree. Transfusions and intravenous alimentation are employed to improve the patient's condition. Forty-eight hours before operation, penicillin is started (50,000 units every three hours). Anesthesia is begun with endotracheal nitrous oxide to permit the use of the high frequency current, thereby saving time in opening the chest. Once the chest is opened, the nitrous oxide is replaced with pentothal, ether, and oxygen. Exposure is obtained by extending the ninth rib. The anastomosis of the stomach and esophagus is done in three layers. Of the forty-four patients found to be operable, 62 per cent survived operation. There was one interesting case in which a second resection was done for recurrence two months after the original operation, and the patient is now apparently in good health. Gastric dilatation occurred only when both vagi were cut at operation and was combated by continuous suction drainage. In the discussion, Dr. Richard Sweet said that he was opposed to inversion and purse stringing the esophageal end of the stomach, since it precluded a secure, neat closure. Reporting an extensive experience at the Massachusetts General Hospital, he said that 69 per cent of the tumors of the lower esophagus were resectable in contrast to 64 per cent for the middle third of the esophagus. The mortality rate was 12 per cent for the lower third and 22 per cent for tumors of the middle third of the esophagus. He advocated excision even when it was obvious that it was only a palliative measure. It was most encouraging to learn that the mortality rate for the cases done in 1945 and 1946 was only 9 per cent. Dr. M. E. DeBakey and Dr. W. E. Adams described methods of enlarging the esophageal hiatus at the site of the anastomosis. Dr. Adams stated that the recent mortality at the University of Chicago was but 17 per cent. His longest survivor has thus far lived fifty months. He suggested that in closing the chest two Foley catheters be employed since their inflatable bulbs permit drainage without plugging. Dr. Adams said that he had one patient living and well nine years after operation. In his last twenty-seven cases, there had been only two deaths. In his experience high resection and anastomosis were no more dangerous than in the lower third of the esophagus.

Congenital Esophageal Atresia and Tracheo-Esophageal Fistula. Clayton G. Lyon, San Francisco (read by Brodie Stephens because of author's illness).—Approximately 468 cases of esophageal atresia with or without tracheal fistula, have been reported. Forty-eight patients have been successfully operated upon. This anomaly has been classified by Ladd into five types of which types III and IV are much the most common. 1. *ese types* consist of a blind upper esophageal stump and the distal esophagus communicating either with the wall of the trachea or its bifurcation at the carina. About 85 per cent can be corrected surgically. In the remaining 15 per cent the esophageal ends are too widely separated to permit re-establishment of esophageal continuity. The presence of frothy oral secretion and persistent regurgitation indicates esophageal atresia. Under the fluoroscope, 20 to 25 cc of lipiodol may be instilled through a small catheter to determine the level of the upper esophageal segment. The lipiodol is then aspirated. Barium should never be used. When a flat plate of the abdomen shows gas in the gastrointestinal tract, it confirms the presence of a tracheo-esophageal fistula (type III, IV or V) and indicates probable operability. The earliest surgical attack on this problem was cervical esophagostomy and gastrostomy, with subsequent construction of an antethoracic esophagus. In 1939, the first successful intra-thoracic esophago-esophagotomy was performed through a right sided extrapleural approach.

out that thrombosis was due to stasis and reduced cardiac output. In closing Dr Maer said that absence of cyanosis indicated that the bronchial artery participated in the shunt rather than the pulmonary artery.

Resection of a Coarctation of the Aorta Followed by Subclavian Aortic Anastomosis. James F. O'Neill, Winston Salem.—Of those individuals with coarctation, "5 per cent die before they are 40 years old. Death may occur suddenly, often in unrecognized cases due to rupture, or cardiac insufficiency and subsequent decompensation, and/or infection. Crafoord's two original cases done in 1914 were described both patients surviving and Gross' experience was related, beginning in 1916, with fifteen cases and but two deaths. Blalock's experiments were noted (1913) in which using anesthetized dogs, the arch of the aorta was divided, the proximal end closed, and the subclavian artery anastomosed to the distal aortic segment. Twenty five per cent of the dogs survived. Excision of the coarcted area and end-to-end anastomosis is the better procedure except when the extent of the excised segment is sufficiently great to cause tension on the suture line. In this situation, the subclavian artery, which is usually dilated, may be employed instead of the short proximal aortic limb, in the anastomosis. Clagett first carried out this maneuver in August, 1916, when confronted with too great tension on the suture line of a proposed aortic end-to-end anastomosis. On Dec. 21, 1916, Bradshaw performed the same operation in a patient presenting the characteristic symptoms of high blood pressure in the arms, low blood pressure in the legs, cold feet, weakness, distended cervical veins, and systolic and diastolic murmurs over the pulmonary area. The approach was through the bed of the fifth rib on the left side. Dr. H. Bradshaw displayed a clamp which he had devised for occluding the aorta and subclavian artery. Surgery is possible in coarctation because the lesion itself is responsible for the development of numerous collaterals, in fact, the subclavian artery is frequently found to be dilated so that it is as large as the aorta. In the discussion, Dr. S. W. Karrington (speaking for Dr. O. T. Clagett) said that the operation was one of necessity rather than of choice. Dr. Clagett has done five cases employing the subclavian artery to restore aortic continuity, four of these were end to end, and one was an end to side anastomosis. In the latter operation, the blood pressure in the arms did not decrease postoperatively. In this series one patient died during his hospital stay. Dr. J. W. Gale suggested that should the subclavian artery be smaller than the aorta the subclavian be transected obliquely to afford a matching lumen. Dr. H. T. Barkley reported a patient who died forty-eight hours after operation with an intact anastomosis where the occluding clamps had fractured the intima and caused a thrombus to form. Dr. L. R. Davidson emphasized the need of turning up sufficient cuff before making the anastomosis. All of the speakers used an everting continuous mattress suture, following Gross' suggestion and practice in contrast to Crafoord who employed a continuous over and over suture.

Aortic-pulmonary Anastomosis for Pulmonary Stenosis, Willis J. Potts, Chicago.—The indications for an aortic-pulmonary anastomosis are the same as those for the Blalock operation, namely, the tetralogy of Fallot. The rationale of both operations is based on need to augment the pulmonary blood flow which is reduced by the pulmonary stenosis. The incision is through the fourth inter-space. By the use of a very ingenious clamp which partially occludes the aorta permitting the flow of blood beyond the clamp a side to side anastomosis is made with the pulmonary artery. The anastomotic hiatus is from $\frac{1}{4}$ inch to $\frac{5}{16}$ inch in length. The procedure has been carried out in twenty seven patients. There were twenty five survivors and of these twenty four were much improved and only one slightly improved. Dr. J. J. Hanson said only one aortic-pulmonary anastomosis had been done at Johns Hopkins.

Diseases of the Esophagus. Paul H. Hollinger, Chicago.—This presentation consisted of an excellent colored moving picture taken through an esophagoscope demonstrating many interesting conditions of the esophagus.

Surgical Management of Carcinoma of the Lower Two-thirds of the Esophagus and Cardiac End of the Stomach, John W. Strieder, Boston.—The chief factor in the improve-

ventilation, consisting of a respirator built into the circuit of a gas machine. The re-breathing bag is contained in a rigid glass cylinder permitting the anesthetist to visualize and anticipate the patient's ventilation requirements. Although the patient is apneic ventilation is adequate. Nitrous oxide and ether are administered endotracheally. No positive pressure is used until the pleura is opened and then never more than 10 to 15 mm, and at a rate about one half of normal. A short period of hyperventilation produces apnea which blocks out stimulation of the respiratory center and permits the anesthetist to assume control of respiration. Dr. Claude Beck said that manual compression of the gas bag was neither dependable nor satisfactory since prolonged manual compression was not conducive to the return of normal function. He considered a mechanical respirator such as Dr. Mautz described, as essential and emphasized the need of adequate ventilation before attempting resuscitation of the heart. Dr. Frederick Kergin said that when prolonged anoxia occurred during intrathoracic operations the contralateral lung might become atelectatic due to mediastinal shift. Dr. Mautz urged again that it was not only necessary to combat anoxia with an adequate oxygen supply but even more important to eliminate carbon dioxide.

The Diagnosis and Operability of Bronchogenic Carcinoma, John H. Gibbon, Philadelphia.—The overall survival rate for both bronchogenic and gastric cancer after surgical extirpation is 22 per cent. Further improvement in the treatment of bronchogenic cancer depends upon earlier diagnosis and more radical surgery. The earliest symptoms were cough, bouts of pneumonia, and chest pain; other symptoms of value were sputum, hemoptysis, weight loss, dyspnea, and wheeze. Fifty-six patients with proved cancer of the lung were seen in the past fourteen months. Exploration was done in thirty-one of these and twenty-one were resectable with but two hospital deaths. Cytologic examination of bronchoscopically removed secretion has proved a valuable aid in early diagnosis. A recent improvement in this technique applicable to secretion from patients consists in instilling salt solution into the suspected bronchus and then aspirating it. In twelve of the patients in whom no biopsy was obtained malignant cells were found in the secretion and nine of these were explored largely on the basis of finding neoplastic cells in the bronchial secretion. Contraindications to surgery are the presence of a hemothorax and metastases outside the involved hemithorax. Paralysis of the diaphragm should not be regarded as a contraindication, nor should a recurrent laryngeal nerve palsy since 10 per cent of these latter occur without satisfactory explanation. He urged a more radical extirpation often opening the pericardium to ligate the pulmonary veins. This is desirable since the neoplasm frequently extends along these vessels. The pulmonary artery is ligated extrapericardially. In this series the tissue resected included portions of the diaphragm in two cases, the phrenic nerve in two, the chest wall in one instance, and the vagus nerve in one. Dr. Peter Herbut, the coauthor, described a larger series of patients (244) from whom 362 specimens were obtained. Eighty-nine of the 244 had proved cancer of the lung. Malignant cells were found in the bronchial secretion of 77 of the 89 patients (86 per cent) while positive biopsies were obtained in 40 patients (45 per cent). He described the Papanicolaou technique. The neoplastic cells are pleomorphic and fall into three categories, namely (1) squamous cell (75 per cent), (2) undifferentiated (13 per cent), and (3) all others (21 per cent) each with well defined cellular characteristics. Wider application of this valuable method of early diagnosis should result in a higher rate of resectability. In the discussion Dr. Michael DeBakey said that biopsy confirmed the diagnosis before operation in two thirds of his cases. In a series of 412 cases 121 patients were considered inoperable and 291 were thought operable, 43 of these refused operation and 1 in 246 exploration was done of this latter group 89 were found to be inoperable (40 per cent). Of those explored 60 per cent were resectable. The mortality rate prior to 1942 was 46 per cent since then it has been 19 per cent. The five year survival rate has been 23 per cent (better than that of gastric cancer). He noted that most patients die within the two year period of recurrence and extension. On the basis of this large experience 2 survive five years out of every 23 patients; however if all 23 were resectable then 5¼ might be expected to survive.

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Cancer of the Lung Relationship of Topographic Features to the Interval and Late Results of Operation, Arthur H. Aufses, New York.—In 1934 and 1931, papers were presented by Dr. Harold Neuhof, reviewing large series of lung tumors from the standpoint of topographical classification. This classification is broken down into three groups: (1) Bronchus tumors (invasive lesions derived from the main bronchi), which are topographically diffuse. They possess marked tendencies to spread in the submucosa and via the lymphatics. (2) Circumscribed tumors (as identified topographically by x-ray view) where lymphatic involvement is limited or late. In this category, lobectomy is often effective. (3) Peripherally invasive (medial aspect more or less circumscribed but invasive of adjacent structures such as pleura, pericardium, or diaphragm). This type often arises from branch bronchi and spreads via the lymphatics. This series comprises fifty-four patients, subjected to pneumonectomy or lobectomy, who survived operation. The follow-up includes a higher percentage of circumscribed tumors (amounting to 25 per cent of all pulmonary carcinomas) because a larger proportion of patients were operable and survived for longer periods. The microscopic features of these tumors bear no significant relationship to the period of survival. Adenocarcinomas were found slightly more frequently in the circumscribed group. In Group 1 (diffuse tumors) there

Group

Group

(23)

was particularly true of main bronchus tumors. Lobectomy is ineffective when there is lymph node involvement but has a place in the treatment of circumscribed tumors. Twenty-eight per cent of the patients in whom lobectomy was performed survived the two-year period. 37 per cent of those in whom pneumonectomy was done survived longer than two years. If patients remain well for two years, it is probable that they are cured. The absence of any correlation between the microscopic picture and the survival period was again emphasized.

Carcinoma of the Lung, Ralph Adams, Boston.—Out of a series of 152 cases of cancer of the lung resection was done in 56 patients, with 8 hospital deaths. Six deaths occurred in the first 17 resections (3 per cent), while there were only 2 deaths in the last 29 (5 per cent). In the surviving 49 patients certain studies were carried out. No patient with undifferentiated (oat cell) carcinoma has lived two years following resection. Of 11 patients living and well longer than one year, 13 were epidermoid in type. Three patients with epidermoid carcinoma grade III (Brodie's classification) have lived over two years and one over five years. Lymph node involvement definitely worsens the prognosis. In the 45 patients 15 had pneumonectomy with 14 (40 per cent) surviving more than two years, including 2 who are living and well after five years, 13 had lobectomy with 6 (46 per cent) surviving more than two years and with 3 living and well more than five years. Only in epidermoid carcinoma did the study reveal that the longer the duration of symptoms prior to resection, the shorter the expected period of survival. In other types the survival period was more closely related to cell type than to any other factor. If the patient survives the first two years after resection he has a 60 per cent chance of cure.

In discussing the previous three papers Dr. Everts Graham said that any statistics

did not be encouraged by any
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of choice. In cancer of the breast some patients have recovered with local excision or simple mastectomy, but the best overall results come from the radical operation. With gland involvement, pneumonectomy should be done. It is frequently impossible to determine the presence or absence of involved glands by inspection alone. They are less likely to be present when the tumor is distant from the hilum. Pneumonectomy rather than partial lung resection, has produced more five-year survivals. Dr. John Strieder stated that smears of aspirated bronchial secretions in cancer of the lung had proved 80 per cent positive. Dr. Jerome Head emphasized the high degree of disability after pneumonectomy.

in patients over 60 years of age. He said that partial lung resection should be given consideration in these cases since preservation of pulmonary function is important. The disability attendant upon pneumonectomy should be considered rather than the operative mortality. He praised the high degree of accuracy in diagnosis which obtained in the microscopical examination of bronchial secretion. Dr Avery reported a series of 50 resected lung cancers. 29 were of the hilar or main bronchus type with 4 patients living, 14 were of the circumscribed type with 5 patients living, and 17 were of the peripherally invasive type with no extended survivals. He reiterated that there was no apparent correlation between cell type and survival period because the degree of malignancy depends upon the "worst" rather than typical cell. Dr John Gibbon urged pneumonectomy as the treatment of choice, but said that there must be surety of diagnosis before any lung is removed. Dr Peter Herbst said that in the last 60 cases of microscopical secretion examination, only 3 had been misclassified. More recent experience would be found bereu

involvement in cancer of the breast. He urged prompt surgical treatment once the diagnosis is made, since slow growing, circumscribed tumors may metastasize or invade at any time.

The Treatment of Inoperable Bronchogenic Carcinoma by Methyl bis, Edward F Skinner, Memphis—Investigations of some 300 nitrogen mustard compounds during the war revealed that they had a specific toxic effect on rapidly growing cells, such as cells of the bone marrow and cancer cells. Since 1942, nitrogen mustard compounds have been used in the treatment of Hodgkin's disease and lymphomas in 126 hospitals. Methyl bis, a nitrogen mustard compound,* is supplied by Memorial Hospital, New York, N. Y., for use under certain conditions of control and study. The hazard of the appeal of treating cancer by "shots" instead of by surgery, where it is indicated, is obvious. There are admittedly a few long-standing survivors after tremendous doses of x-ray for bronchogenic carcinoma, but this is contrary to the general experience. Forty patients with bronchogenic carcinoma have been treated but this report covers seventeen treated during the preceding year. These cases were unsuitable for surgery because of distant metastases. Some of these patients have shown improvement which could not be derived from any other treatment at our disposal, including x-ray therapy. The benefits last for several weeks to several months. The greatest improvement occurs after the first treatment, subsequent treatments are progressively less effective until finally they are of no help at all. There were no toxic manifestations, aside from nausea and vomiting and anorexia for the first twenty-four hours after treatment which were at least partly eliminated by the injection of 100 mg. of pyridoxine at the time of therapy. The tumors remain stationary for variable periods of time, as corroborated by x-ray views, and then later resume growth. In some cases methyl bis was given at the same time as x-ray therapy but without improvement in results. It is possible that the doses of methyl bis were inadequate, but doses twice as large as the standard dose produced no better results. There was a greater gain in weight on methyl bis alone, than when x-ray was used as an adjunct. It is desirable to give as large a dose as the patient will tolerate. Clinically, the results are better than x-ray therapy in addition it is cheaper and can be given in the office. It is conceded that the results in lymphoma are better than those in bronchogenic carcinoma. Methyl bis comes in 10 mg. vials, which are diluted with 10 cc. of normal saline solution. The dose is 0.1 mg. per kilogram of body weight given intravenously in split doses over five consecutive days or five days apart. Ten cubic centimeters of normal saline solution are given immediately after the methyl bis injection. As an office procedure, methyl bis is given once a week. It can also be administered during a saline infusion by injection through the tubing.

*Manufactured by Merck & Co. Inc. Manufacturing Chemists Rahway N. J.

In the discussion Dr Michael DeBakey reminded us that the same apparent clinical improvement in inoperable cancer cases may be obtained by a similar increased interest in improved morale and better care of such cases. Dr Fred Harper told of ten patients with inoperable carcinoma who had been treated with methyl bis. Three had died showing some necrosis of the liver. Seven were still living two with obvious metastases in one the metastases had disappeared. One patient had coughed up plugs of tumor tissue. Methyl bis seemed to reduce cough and pain. Dr Avery said that methyl bis had been used at the Hines Veterans Hospital in nine cases of pulmonary cancer, six patients seemed benefited as evidenced by the need for fewer hypodermics. In one instance a superior vena cava obstruction had disappeared while undergoing treatment. Dr Ogler Abbott said that he had used methyl bis in five patients but that without the psychotherapeutic influence gained by having the patient know something new was being tried on him he had observed no benefit.

Nonmalignant Lesions of the Lung Simulating Bronchogenic Carcinoma. Report of Thirty Cases. Lyman A. Brewer III, Los Angeles.—During the past six years 300 patients with bronchogenic carcinoma have been seen but only 40 per cent yielded a positive biopsy at bronchoscopy. In the remainder diagnosis was made by clinical means, often exploratory thoracotomy. Hence only a small ratio of these patients (23) were operable. The desired goal has been earlier and earlier diagnosis. This led to exploration in many patients without a proved diagnosis of pulmonary cancer. Thirty patients were operated upon for suspected malignancy, in whom the lesion was beyond the range of bronchoscopic vision, 27 had resections of some type and 1 who refused resection later had a thoracoplasty. All 30 cases presented benign lesions which fell into three groups. The inflammatory group consisted of pulmonary abscess, nonspecific granuloma, tuberculosis, and echinococcus disease. The benign tumors were adenoma, lipoma and fibroma. The congenital conditions included lung cysts and an intrathoracic thyroid. Bronchogenic carcinoma occurs five times more frequently in males than females; in the benign lesions the incidence is the same in both sexes. The x-ray picture may reveal a central or peripheral mass, an atelectatic lobe, a cyst or abscess. Most of these patients will have been cured only by pulmonary resection. Such experience should encourage the surgeon to resect peripheral pulmonary lesions in which bronchogenic carcinoma is suspected. If carcinoma is found resection offers the only chance of cure. If the lesion is nonmalignant this study demonstrates that in most instances the pathological condition is one that can be cured by resection.

In discussing this paper Dr Everts Graham urged that exploratory thoracotomy be done oftener. All tuberculosis should be resected since they may become active and produce a bilateral spread. Dr David Waterman said that a sputum positive for tuberculosis may mask a carcinoma and that it was unwise to put too much weight on a single sputum examination even though positive. Dr Frederick Mautz reported a case of gumma of the lung which is exceedingly rare in which the Wassermann test was not reported until after operation. Dr Edgar Davis said that all solitary spherical intrapulmonary lesions should be explored even if one is unable to make a clinical diagnosis. In 40 such cases he has performed 39 operations and found 10 per cent of them to be malignant. Twelve of these patients were without symptoms yet 8 of them had a significant lesion. Many cysts are malignant. Dr Richard Sweet also urged frequent exploratory thoracotomy but said that even after exploration diagnosis was not easy. He advised doing biopsies at the time of exploratory thoracotomy. Chronic pneumonitis may be very difficult to distinguish from bronchogenic carcinoma. Dr Lincoln Brown said that lipo-pneumonia was progressive and should be resected. Dr Brewer counseled more explorations and segmental resections.

Specialism in Surgery. I. A. Bigger, Richmond, Va.—The identical Address.—Specialism in medicine dates back to antiquity. Preference to specialism are found in accounts of ancient Greek and Egyptian medicine. Specialism cannot have disappeared in the Middle Ages possibly because of the academic and philosophical aspect of medicine as it was taught at that time. In the nineteenth century the development of new instruments and techniques afforded a rational basis for the beginnings of specialism as known today. Ophthalmology

appeared first, in 1851, followed by urology in 1871. Other specialties developed slowly until the 1890's. Bevan, twenty five years ago, asserted that one third of all physicians professed to be specialists. The delimitations of specialties are changing. In 1937, Rankin said that the general surgeon of today lives in the afternoon of his career. Halted advocated the training of a well rounded general surgeon. Barker pointed out that specialization was the logical consequence of the division of labor, and that it should increase the productivity and fruits of labor. It was feared that specialization would lead to lower standards, less intellectual ruggedness, and a narrow outlook with loss of the over all picture. A broad training in basic science designed to cultivate breadth of vision must be the foundation for training in any specialty, if the broad perspective and wise understanding shall persist. The ideal concept envisions an organization where consultation, conference, and cooperation between those trained in various specialties is routine, carried on hand in hand with fundamental research. The present specialty boards indicate certain trends. The prescribed periods of training are perhaps too rigidly fixed. It might be well to allow credit for work done in other fields to refute the criticism of regimentation and narrowness in such prescribed training. It is well to remember that when any type of training becomes established by custom, it may assume legal stature.

Pulmonary Edema. Experimental Observations on Dogs Following Acute Peripheral Blood Loss. Robert M. Eaton, Grand Rapids (Rose Lampert Graff Prize Essay).—These exceedingly important and fundamental experiments were the result of the author's interest in the effects of blood loss and were carried out while he was in charge of the St. Louis Blood Bank during the war. Acute peripheral blood loss alone will produce changes in the lungs consisting of edema, hemorrhage, vascular congestion and endothelial damage, which in turn cause a block to normal circulation. Because of the stasis in the pulmonary circuit, an acute systemic circulatory imbalance occurs in which arterial pressures are low and venous pressures high. The lung changes following peripheral blood loss are not transient and may last five days. Dogs were bled 25 per cent of their estimated normal blood volume and certain observations were made. Using the photographic Wigger a manometer and the kymograph simultaneous direct pressure readings were obtained from the femoral artery, the femoral vein, and the pulmonary artery. After the induction of hemorrhage all pressures dropped, but this was followed by a temporary pressure elevation in the venous system (femoral vein and pulmonary artery) without any rise in pressure in the peripheral arterial system. These findings were probably due to stasis and increased back pressure in the pulmonary circuit. Employing a technique of lung desiccation a predictable pattern of pulmonary moisture change was noted. It was elevated during the first 20 minutes, became subnormal at 45 minutes, was above normal at 1½ hours and then leveled off to normal 4 hours after the blood loss. Using the same technique pulmonary edema was found to be aggravated by the infusion of normal saline solution but not by the administration of blood or plasma. During the first three hours after hemorrhage plasma protein levels were low and hematocrit readings high. Another interesting observation was that as a result of blood loss there was an immediate increase in pulmonary lymph flow as judged by cannulization of the pulmonary lymphatic (right thoracic) duct. Microscopic sections were made which gave corroboratory histologic evidence of alveolar and tissue edema and hemorrhage. The initial hemorrhage causes an anoxia which damages the alveolar capillary endothelium resulting in an increased permeability to fluids which in turn produces the edema, congestion and interstitial hemorrhage. Rapid deep breathing augments the negative intrathoracic pressure and increases the already present pulmonary edema and hemorrhage as the great veins of the thorax become overdistended. In combating the effects of a massive peripheral hemorrhage anoxia should be overcome by giving whole blood, never saline solution, and the administration of oxygen under pressure so that it may penetrate the film of water, coating the alveoli.

The Effect of Pulmonary Inflation and Deflation Upon the Maintenance of Circulation. Samuel Alcott Thompson, New York.—Active inflation and deflation of the lungs causes a compression and distention of the pulmonary capillaries, which sets up an artificial circula-

tion in the normal direction over the entire body, without benefit of any heart activity. Such movement was demonstrated in dogs, immediately after death by the use of radioactive sodium, fluorescein, and oxygen. Dogs were anesthetized with intraperitoneal nembutal, and 2 to 5 c.c. of heparin were injected. Ten minutes later, the endotracheal tube was clamped for twenty or thirty minutes, on releasing the clamp, a resuscitator was started and the tracer substances injected. After radioactive sodium was injected into a femoral artery or vein, its presence could be demonstrated in a brief interval, by use of a Geiger counter, in specimens obtained from the carotid artery or the femoral artery of the other leg. Using fluorescein (2 cc. of 5 per cent solution), which emits a golden green glow when exposed to ultraviolet light, its presence could be easily seen in the skin, mucous membranes, the coronaries, and brain. Blood samples for the determination of oxygen saturation were taken from the femoral artery at the beginning of the experiment, again shortly after clamping the endotracheal tube, and forty five to sixty minutes after resuscitation had been carried on. The only possible source of oxygen was the pulmonary capillaries as they filled and emptied with alternating inflation and deflation of the lungs. Within ten minutes of asphyxia, by the use of resuscitation, the oxygen saturation of the blood in the femoral artery regains the pre-asphyxial level. Unless clotting is prevented by the use of heparin, there can be no circulation. Heparin prolongs the time available of the blood. It sustaining quantity during a given period are 100 per cent more efficient than either inflation or deflation alone. The pumping action is the result of the compression and dilatation of the pulmonary capillaries.

The Regeneration of Defects of the Trachea and Bronchi. An Experimental Study. Rollin A. Daniel, Jr., Nashville.—In 1940, Cappel showed that a tracheal defect could be repaired with fascia which was later transformed to collagenous fibrous tissue. Since fascia is not rigid, it is unsuitable for experimental procedures in tracheal segments of the tra-

defects were bridged by flanged tubes (8 to 10 mm. in diameter) of vitallium, steel, etc., which were tied into the divided ends of the trachea with encircling braided silk ligatures. The mediastinal pleura was closed over the repair. The animals were sacrificed at intervals from two weeks to a year. They tolerated the presence of the tubes well. The beginning regeneration of cartilaginous rings is evident at two weeks, and, with time, the regenerated rings very closely resemble those which were removed. The new connective tissue cells differentiate into cartilage cells. The lining epithelium also regenerates slowly, and resembles ciliated columnar epithelium, being composed of a thin layer of small cells which appear to be stratified. There is no regeneration of cilia or goblet cells. Dr. Stuart Harrington described a similar technique for the repair of tracheal defects, however, using plastic tubes.

An Improved Method of Resection of Pulmonary Segments. Report of a Technique Used in Over Sixty Cases of Bronchiectasis. F. M. Woods, Boston.—Pulmonary diseases amenable to resection often involve segments of lobes as well as entire lobes. It is desirable to preserve the normal segments of lobes as functioning units. When the disease is extensive, involving multiple areas, the conservation of all healthy segments is essential for optimum function. This method based on the individual ligation technique, applies this procedure to artery, vein, and bronchus of the pulmonary segment. It facilitates the visualization of the segmental planes of cleavage, permitting the separation of diseased and healthy segments without damage to the latter. In bronchiectasis particularly, this conservation of healthy lung tissue has broadened the scope of resective surgery to include many more patients with extensive bilateral disease than were feasible when lobes were regarded as surgical units. Although segmental resection does not replace lobectomy it has proved a valuable adjunct, especially for the patient with multilobar disease. In the past thirty months seventy segmental resections have been performed fifty for bronchiectasis and twenty for other conditions, which include cysts, tuberculomas, and benign tumors. In seven patients, multiple

bilateral resections have been carried out, usually the basal segment and lingular segment on the left, and the basal segment with middle lobectomy on the right. The technique of the operation was shown in an excellent movie, and its great value lies in the preservation of functioning lung tissue in an otherwise badly diseased lung. Dr Herbert Adams pointed out that Dr E. D. Churchill had initiated segmental resections in 1937. In seventy-three segmental resections, there had been six bronchial fistulas (all in lingulectomies) but they had all healed spontaneously. Dr David Waterman emphasized the importance of conserving good lung tissue, in spite of occasional leaks from raw surfaces and atelectasis in the remaining lobar segment. Atelectasis of the remaining portion of a lobe, especially of a lower lobe, can be avoided if the remnant is kept in its proper position by suture. It is important to ligate segmental bronchi high up, so that there is an stump or only a very short stump. This method is prone to leave exposed raw lung surfaces and every effort should be made to cover them with pleura.

The Place of Exploratory Thoracotomy in the Management of Intrathoracic Disease, John B. Grow, Denver.—This study shows that there should be no hesitancy in advocating exploratory thoracotomy for all obscure intrathoracic lesions. It is a safe procedure with low morbidity, and in this series of cases there were no deaths. One must adopt an attitude of readiness to explore the chest when the usual diagnostic procedures fail, as is so frequently the case with upper lobe lesions beyond the reach of the bronchoscope. Of 200 lesions which were explored, 21 per cent proved to be malignant. In this series, there were 113 intrapulmonary lesions, of which 29 (25.6 per cent) were malignant. There were 86 cases in which the lesion was described as "circumscribed," and 20 (23 per cent) of these were malignant. The remaining cases of this group consisted of 37 instances of tuberculosis (24 were tuberculomas), 13 lung cysts, 3 coccidioidal granulomas, 3 diaphragmatic hernias, 2 liver abscesses, 1 echinococcus cyst, and 1 arteriovenous aneurysm. Forty-four operations were performed for cancer of the lung, only 45 per cent of these had been diagnosed by bronchoscopic biopsy. A high percentage of chronic abscesses of the upper lobes are due to intrabronchial neoplasms which should be treated by exploration and resection, instead of the common practice of drainage. Diagnostic radiation therapy should be abandoned in favor of obtaining tissue for pathologic diagnosis before instituting any type of therapy. The effect of x-ray therapy on tumors of the lymphoma group is not uniform since not infrequently Hodgkin's disease proves radioresistant. Exploratory thoracotomy is without risk, all deaths in this series were the consequence of the surgical treatment of the underlying condition. There were five deaths after pneumonectomy and one after lobectomy. Exploration in 35 patients with suppurative disease (chronic abscess) revealed 11 (31 per cent) with bronchogenic carcinoma.

Chronic Nonspecific Suppurative Pneumonitis W. E. Adams, Chicago.—The etiology is not known. Its onset is insidious and it runs a very chronic course. The duration of symptoms in the ten patients reported here ranged from six months to twenty-two years, the duration in the majority of the cases was from two to ten years. All the patients were over 30 years old. There is usually a productive cough with episodes of hemoptysis accompanied by low grade toxicity as evidenced by fever. There may be some pain. X-ray examination reveals an ill-defined opacity extending out from the hilum region without cavity formation. The condition may be located in any part of the lung, and at times is bilateral. It must be distinguished from pulmonary tuberculosis, bronchogenic carcinoma, nontuberculous lung abscess, and bronchiectasis. The pathologic picture is one of chronic, diffuse inflammation, showing marked fibrosis which is responsible for narrowing of the bronchial lumen and atelectasis. Other features are thickening of the alveolar walls. Lymphoid hyperplasia, lymphocytic and plasma cell infiltration, and the presence of fat-filled macrophages in the alveolar spaces. Clubbing of the fingers does not occur. In short, the condition is characterized by its insidious onset, chronic course, and pulmonary inflammation without abscess formation or bronchial dilatation. Of the ten cases, five were treated by lobectomy, two by pneumonectomy, two by drainage. In one bilateral case, only biopsy was done. Dr Robert Jones pointed out the similarity of this condition to chronic hypoid pneumonia in which the lung shows marked fibrosis and a high fat content. Dr Ralph Bettman told of a case of nonspecific suppurative

pneumonia which presented the picture of lung tumor but responded to x-ray therapy. In closing Dr. Adams said that x-ray therapy might be effective if given early in the disease. Although he employs chemotherapy in these cases, he urged that resection be done because of the difficulty in differentiating it from carcinoma. Lobectomy usually sufficient.

Pulmonary Resection for Chronic Abscess of the Lung. Donald L. Paulson, Dallas—In 1941 the co-author Dr. Robert Shaw had advocated a one-stage lobar resection for lung abscess as soon as the diagnosis was made. In view of the fact that chronic lung abscesses are often multiple involving more than one lobe and may be productive of marked fibrosis throughout a lobe or lobes, the likelihood of any drainage operation being such a condition a very small. A series of 86 patients was presented, 50 of whom had had resection for chronic lung abscess with a reduction in mortality to 3 per cent in contrast to a 13 per cent mortality in 1941. The rate of cure has risen from 57.6 per cent in 1941 to 80 per cent in the present series. Drainage operations should be reserved for a late abscess used as an expedient in the very ill patient and also to reduce the size of large abscesses in the hope of conserving functioning lung tissue. Resection was done in abscesses of long duration (two to eighteen months) and when the abscesses were multiple. Resections were complicated by postoperative empyemas in 29 per cent of the cases. Surgical drainage and pulmonary resection for chronic lung abscess should be regarded as complementary in the treatment of this condition.

Pulmonary Resection for Chronic Lung Abscess. Edward M. Kent, Pittsburgh—This report is an analysis of thirty consecutive cases of chronic lung abscess treated by pulmonary resection. Males outnumbered females in a ratio of five to one. Age ranged from 17 to 64 years with an average of 33 years. The duration of the lesions varied from 4 to 48 months with an average duration of 15.8 months. The cases were divided into three groups. Group I consisted of eleven cases of multiple abscesses involving all the lobes of a lung; the patients were treated by pneumonectomy. There was one death on the ninth postoperative day from a diffuse pneumonia in the remaining lung; there were no postoperative empyemas and only one transient bronchial fistula. In Group II there were eight cases of multiple abscesses confined to a single lobe. Seven of the patients were treated by lobectomy without a complicating empyema or bronchial fistula. The eighth one died on the operating table of asphyxia resulting from a severe hemorrhage in the involved lung before the affected lobe could be mobilized. Group III consisted of eleven cases of solitary abscesses confined to a single lobe and the patients were treated by lobectomy. There were no deaths in this group; a single bronchial fistula occurred which was followed by an empyema. Seven patients in the entire group had been subjected to previous drainage without improvement; five were in the multiple abscess group (I and II) and two were in the solitary abscess group. The operative mortality was 6.7 per cent. The low incidence of postoperative empyema (one case, 3.3 per cent) was the result of the application of the indwelling catheter technique which minimizes bronchial fistula and of the use of penicillin before, during and after operation. In the late solitary abscess surgical drainage still has a role but in the chronic multiple lobular multiple abscess drainage is wholly unsatisfactory because of the high mortality, long mortality tendency to recur and frequency of re-drainage.

In discussing these two papers Dr. J. D. Moody emphasized the need of preventing the spread of infection from the pleural space and hence an ingenious apparatus for plugging the bronchus consisting of a balloon, an umbilical catheter and a hypodermic needle.

Dr. J. D. Moody also discussed the difficult problem of exsanguination. He used an iron lung for the lead and operated on one lobe at a time. He said that the justification for the increased safety in lung resection was a suppurative disease. Bronchial stump should be trimmed very short because long bronchial stump after postoperative empyema. Dr. A. R. Curreri advised the use of Trenchard's suture on the outside of exsanguination. Dr. E. J. Grace pointed out the effects of the use of aerosol when a patient is wetting again.

in reducing secretion before operation. He spoke of the synergism of penicillin and streptomycin but urged that large amounts be employed. As a wetting agent or detergent, he used 3 cc of zephiran (1 to 1,000 solution). Dr J K. Poppe observed that it was often difficult to differentiate chronic abscesses from bronchiectasis. Operations on patients with poorly draining abscesses carried a risk twice as high as those for bronchiectasis. The better epithelialized the abscess cavity, the lower the risk. Dr O C Brantigan said he used the face down position, and utilized the cerebellar headrest and shoulder braces. Dr Donald Paulson said that because of the individual ligation technique, there had been no contralateral spread and only one ipsilateral spread, and this probably a direct extension to a middle lobe after an upper lobectomy. Dr Kent emphasized the value of the prone position and the importance of an immediate available bronchoscope during these resections to open a plugged bronchus and prevent asphyxia.

The Effect of Chemotherapeutic Agents on the Growing Tubercle, Robert G. Bloch, Chicago.—It is known that streptomycin inhibits the *in vitro* growth of the tubercle bacillus. However, because of the absence of blood supply, streptomycin does not penetrate the centers of necrotic areas. The effect of various chemotherapeutic agents were investigated (1) by the influence of such agents on the tubercle bacillus growing in culture employing the culture technique of Dubos and Davis (1946). The tubercle bacillus is grown in a liquid medium, which produces an active, sub-surface, diffuse submerged growth, which three days after inoculation can be read on the colorimeter. One cubic centimeter of streptomycin completely inhibits the growth of 0.4 micrograms of the culture. The addition of ferric ammonium citrate does not enhance the effectiveness of the penicillin. It has been shown histologically that iron does not enter the tubercle. (2) Investigations regarding the influence of streptomycin on normal tissues (namely in rabbit). Streptomycin when injected intradermally irritates the skin of animals producing sometimes necrosis but chiefly a nonspecific inflammation with abundant immigration of eosinophiles, followed by induration and fibrosis. The skin irritations caused by streptomycin alone appear more severe than those caused by tuberculous infection but microscopic examination proves them to be very superficial, causing much less tissue destruction than in streptomycin treated or untreated tuberculous areas. It has been observed clinically that nebulized streptomycin inhalations cause marked irritation of the bronchial mucosa. This observation was confirmed by exposing rabbits to aerosol streptomycin inhalations over various periods of time. The aerosol globule, which is 2.5 microns in diameter, is ideal for penetrating the lungs. (3) The development of tuberculous lesions was not influenced by streptomycin when treatment was begun as early as four days after inoculation with the bacillus. Streptomycin was given intradermally to rabbits in doses of 0.1 to 0.5 mg at the time of inoculation and four and eight days afterward. The skin irritating effect of streptomycin was again noted. Caution was inhibited only when the streptomycin injections were begun immediately after inoculation. A bovine strain was used routinely, but in a few instances when lesions were produced by human strains, the inhibitory effect of streptomycin was considerably greater and was effective even when treatment was not begun immediately after inoculation. Examination of sections for acid fast bacilli showed considerable reduction in the numbers of organisms in caseous and noncaseous infected areas where treatment had been coincidental with inoculation. There was no appreciable reduction in the numbers of bacilli found where the administration of streptomycin was begun four days or longer after inoculation. Radioactive phosphorus has a special affinity for the caseating tubercle when injected into an organ or tissue the phosphorus will penetrate the tuberculous area.

Closed Intrapleural Pneumolysis. An Analysis of 1000 Consecutive Operations, J. Claude Day, Detroit.—This report covered 1,000 consecutive operations done in the last seven years at the Herman Kiefer Hospital and the War H. Maybury Sanitarium. While intrapleural pneumolysis has enhanced the effectiveness of pneumothorax, certain undesirable complications are attendant upon its universal use. It should not be regarded as an innocuous procedure to be employed routinely whenever restraining adhesions, no matter how complex, are present. The overall mortality rate was 13 per cent. The complications were

the development of persisting effusions (199), empyemas (50), and the obliteration of the pleural space (63). Sixty-five cases were abandoned because of extension of the disease or ineffectiveness of the pneumothorax. Complications were more frequent when pneumonolysis could not be completed, and when the cavity was apparently increasing in size. Late complications were more numerous than early ones. The results in 472 cases were described as effective. There were 5 deaths at the time of operation and 161 later deaths, of which 110 could be ascribed to complications. The operation should be restricted to unilateral tuberculosis where the amount of parenchymal damage indicates the need for prolonged collapse. Intrapleural pneumonolysis should not be performed in the presence of tuberculous empyema, acute pleurisy with effusion, or extensive parenchymal tuberculosis, nor should it be done when there is pleural symphysis or adhesions arising from the periphery of thin-walled cavities.

In the discussion, Dr. Edward Wells said that these deaths were not due to pneumonolysis but to the underlying disease. There should be no mortality from the operation alone. Many of the patients would have died but for the pneumonolysis which rendered a pneumothorax effective. Dr. Julian Moore questioned the validity of the reasoning by which the over-all 18 per cent mortality rate was arrived at, he pointed out that 18 per cent was the approximate mortality rate of all late cases of tuberculosis. He felt that the actual mortality rate that could be directly ascribed to pneumonolysis was about 15 per cent. Dr. Louis Davidson stated that there was a wider field of vision obtained when using the two-convex thoracoscope than with the single-convex type, such as Dr. Day had employed. The two-convex thoracoscope permits distinction of weblike adhesions from the parietal pleura. In a series of 192 in effective pneumothoraces, satisfactory collapse had been achieved in 73 per cent by intrapleural pneumonolysis with only 84 per cent of complicating empyemas. The incidence of empyema as a complication of pneumothorax (30 to 20 per cent) is greater than in pneumonolysis. Dr. E. J. O'Brien urged the importance of evaluating the late, rather than the early results of pneumonolysis. He felt certain that ultimate results in this type of patient would be better if more thoracoplasties were done and fewer pneumonolyses. Dr. Day said that the aim of pneumonolysis was the conversion of an incomplete collapse to an effective one and he hoped that by the observation of certain indications patients to whom pneumonolysis was performed should enjoy the same outcome as those on whom pneumothorax alone was done.

Preliminary Anterior Chondrocostectomy Combined With Closed Cavity Drainage and Thoracoplasty

Edward S. Wells, Sarasota, Fla.—The conventional thoracoplasty

closure of the anterior rib segments may bring about further reduction in cavity size. Revision operations which are difficult and dangerous have not appreciably altered the results. It was hoped that the combination of the Monaldi cavity drainage (1936) with thoracoplasty might produce the desired results. To avoid the risk of sinus wound infection which might arise from the sinus tract of the drainage tube, it was deemed wise first to do an anterior chondrocostectomy. The size of the giant cavity was distinctly diminished after the anterior operation. This was then followed by a conventional first stage posterior thoracoplasty. Such surprising collapse of the cavity occurred that it was decided to postpone drainage once more and do the second posterior stage. In the first six cases complete closure of the cavity resulted. The next case proved a failure and the resulting change in size and shape of the cavity made later drainage hazardous and impossible. Since then a number of cases have been done pursuant to the original plan, namely, the drainage tube is inserted about two or three weeks following the anterior stage. Suction is then started and the posterior stages performed one month later. To date there has been complete cavity closure in all cases. In some the tubes have been removed and the cavities have remained closed, others are still on suction. It is left up to determine or estimate how long the drainage tube should remain in place. Perhaps when the drainage is constant and no evidence of cavity can be seen by x-ray examination and the patient is free of sputum, the tube might be removed. This combination of operations affords a more effective method of closing giant cavities than any previous technique.

Book Reviews

Human Torulosis A Clinical, Pathological and Microbiological Study With a Report of Thirteen Cases. By L. B. Cox, MD (Melbourne), MRCP (Edinburgh), FRACP, and J. C. Tolhurst, MSc (Melbourne). Pp 149, with 67 illustrations. Melbourne, 1946, Melbourne University Press.

Torulosis, also known as cryptococcosis, is an infection due to a yeast which has a tendency to invade the central nervous system. In their classical monograph, *Torula Infection in Man*, Stoddard and Cutler in 1916 designated the etiologic agent as *Torula histolytica*. The present monograph is a scholarly presentation of the subject by two Australians, one a neurologist and the other a bacteriologist. Although the disease has been considered to be relatively rare, one of the authors has encountered eleven cases since 1936 in southern Australia. Their purpose in this work is to present thirteen unrecorded cases of human torulosis with meticulous clinical and pathologic descriptions and to define the characteristics of the causative organism with the results of animal inoculation. In addition, they have brought the literature on the subject together. Without any doubt, this represents the definitive statement on the subject. It is not unlikely that many cases of torulosis are being overlooked, and this volume may serve as a stimulus for clinicians to consider the possibility of torulosis in any ill defined case of encephalomeningitis with and without pulmonary manifestations.

One of the intriguing features of torulosis as emphasized by the authors is a general sized enlargement of the lymph nodes which present evidence of Hodgkin's disease. They believe that this association is more than coincidental and on page 62 state, "We believe that chronic torulosis may result in glandular enlargement, and occasionally in true Hodgkin's disease." And elsewhere, on page 126, "Hodgkin's disease which occasionally complicates torulosis is a separate disease initiated from the infection." In this connection, it is of interest that American workers have recently implicated *Brucella* as a cause of Hodgkin's disease. Apparently experimental torulosis in lower animals is not associated with the granulomatous lesion of Hodgkin's disease.

While the monograph reflects the postwar shortage of high grade paper, the 67 illustrations are excellent reproductions. The index is very comprehensive, and this with the bibliography should be of considerable aid to students of the disease.

Tentative Operatoires Dans le Traitement de Certaines Psychoses By Egas Moniz, Professor de Neurologia, Lisbonne. Masson & Cie.

This book was published in 1936 after twenty patients had been treated by injection of alcohol into the central white substance of the prefrontal lobe or by cutting the same white matter with an instrument which Moniz calls a cerebral leucotome. This leucotome is inserted into the white matter, then a central wire core is pushed into the trocar so that a loop projects near the distal end and by rotating the instrument spheres of white matter 1 cm in diameter are separated. These injections and spherical leucotomies of the original operations have since been modified by others and have become known as prefrontal lobotomy.

The book consists essentially of three parts.

The first part is a discussion of the considerations which led to the introduction of these operations. It consists of a discussion of cerebral localization, the function of the frontal lobe, and a consideration of normal and abnormal emotional reactions.

It is concluded that the emotional life is a summation of the physiologic activity of the nerve elements of the brain in which the frontal lobes have an especially important role.

Extensive nerve cell centers and their connections by rapidly forming new and successive composition or functioning *circuits* are the anatomic physiologic basis of the normal emotional life. In the normal person these combinations rapidly change, but if these connections become more or less fixed, the patient suffers from depression, hypochondriac ideas of guilt or persecution or develops an anxiety state.

The destruction of parts of the central white substance in the frontal lobe was instituted to destroy or break up these fixed pathways in the emotionally disturbed patient.

The second part of the book consists of a very detailed report of each of the twenty patients on whom operation had been done.

The third part of the book is a discussion of the technique and results of operations. The modifications made in the technique as experience was acquired are described and discussed. An attempt is made to correlate the location and extent of the destructive lesion with the result obtained. It is even suggested that the fibers affected in hypochondriasis are in the medial part of the frontal lobe and those involved in depression in the central part.

It was noted that it was two to four weeks before some patients reached the maximum improvement. Many general reactions were noticed as a result of these operations, such as pain when the central white substance is destroyed, and after operation some complained of headache and many vomited and became somnolent. Also noticed after operation were many neurologic symptoms such as fibrillary twitchings, loss of sphincter control and diarrhea, miosis, and anisocoria.

Psychic changes noticed after operations were apathy, loss of initiative, stereotyped movements, catatonias, mutism, and many others.

The book is of historical interest but these early operative methods are now quite obsolete. Many authors are referred to by name, but no references are given.

Textbook of Gynecology By Arthur Hale Curtis M.D. Professor Department of Obstetrics, Northwestern University Medical School. Pp 755 with 433 illustrations. Philadelphia, 1946, W. B. Saunders Company. \$4.

This textbook continues to be one of the best of its kind. The splendid description of pelvic anatomy is unsurpassed in any textbook. This continues to be one of the outstanding features of the book. Almost everyone is familiar with the previous editions consequently comment is reserved for the changes which have been made.

The author has changed the sections concerning endocrinology and its relation to uterine bleeding. The chapter dealing with gonorrhea has been reorganized with special reference to the new therapeutic agents. The section on streptococci of the pueris has been extensively and well rewritten. The author has also rewritten the chapters dealing with the Brenner tumor and with teratomas. A completely new heading concerning the adrenal like tumors of the ovary has been added. The author has very wisely stressed the importance of urinary incontinence and illustrates methods of repair. He mentions a bit about the importance of the Rh factor in repeated transfusions. However one wishes that more emphasis might have been given to the problem of the Rh factor in general—especially the importance of preventing sensitization of girls and women to the Rh bearing age.

This book continues in its high place as a text and can be recommended.

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SURGICAL CURE OF INNOMINATE ANEURYSM

REPORT OF A CASE WITH COMMENTS ON THE APPLICABILITY OF SURGICAL MEASURES

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ANEURYSMS of the innominate artery present a difficult problem in therapy and there are few reported instances of surgical cure. Excluding such auxiliary measures as wiring, distal arterial ligation, and the production of a distal arteriovenous fistula, thirty-seven attempts at direct operative attack have been recorded. Only nineteen of the patients so treated have survived the procedure and not all of them have been cured. It seems desirable, therefore to report another successfully treated patient and to inquire into the applicability of surgery in such lesions.

CASE REPORT

The patient was a 25-year-old soldier who had been struck in the suprasternal area by a small shell fragment on July 14, 1944. There was no external bleeding. Two thoracenteses were required because of right hemothorax. For a while he progressed satisfactorily but nine days after injury when he was told he was being returned to duty he became very hoarse. For some days he was unable to speak at all. He was transferred to several replacement centers and hospitals including a psychiatric institution until finally in November, it was discovered that he had a right recurrent laryngeal paralysis and a mass in the anterior mediastinum. Up to this point it had been thought that his complaints were on a functional basis. He arrived in the Zone of the Interior on December 10 and at the Mayo General Hospital on December 22.

The patient had retained normal voice. He complained of a constant sense of oppression which was accentuated by forward leaning, and which was felt in the upper anterior part of the chest. He breathed normally without discomfort but experienced substernal pain on deep inspiration. There was some difficulty in swallowing dry foods. He attributed his thirty-pound loss of weight to poor appetite. He complained of some weakness of the right upper extremity and noted that it was often darker in color than the left and that the veins of the right hand appeared distended as compared with those of the other hand.

Examination revealed a tall thin somewhat apprehensive young man who was in no distress. The general examination was not remarkable. No mediastinal mass was evident on percussion. In the right suprasternal fossa and to a lesser extent in the suprasternal arch and over the upper sternum and to the right of it a local systolic bruit was audible.

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Pulses in the upper extremities were about equal in forcefulness. Blood pressure was 134/85 in the right arm, 146/90 in the left. The veins of the right hand were somewhat distended. No color changes in the extremities were noted and sweating was normal. In a room at 22° C the fingers of the right hand were from 2° to 3° C cooler than those of the left.



Fig 1



Fig 2

Fig 1—Roentgenogram taken shortly after admission. A shadow compatible with that of an innominate aneurysm is seen.

Fig 2—Roentgenograms taken eight days after the first operation. The mass is no longer visible.

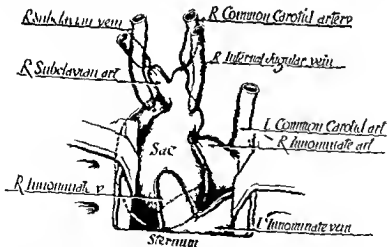


Fig 3—Schematic diagram of the aneurysm.

Oscillations were equal in the two arms on oscillography slightly less at the right wrist than at the left. Ergometry revealed some weakness of the right hand. Laryngoscopic examination showed paralysis of the right vocal cord. Electrocardiograms were normal. Roentgenograms demonstrated a mass in the upper right section of the anterior mediastinum (Fig 1).

The impression was held that the patient had a traumatic innominate arterial aneurysm and a right recurrent laryngeal palsy. He withstood prolonged right carotid compression repeatedly without difficulty.

On Feb. 15, 1945, under intratracheal anesthesia, exploration was carried out through a sternal splitting incision. The sternum was divided down to the level of the third interspace and across into the interspace on both sides. A large sacular aneurysm of the

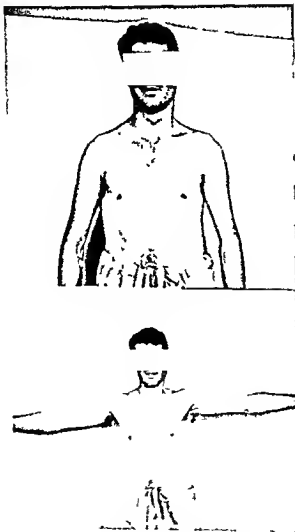


Fig. 4.—Postoperative photographs of the patient. The contour of the chest is normal and shoulder movements are not restricted.

innominate artery was found involving a considerable length of this vessel and beginning about 2 cm distal to its origin. The artery was occluded proximally with a rubber-hol clamp. The right hand immediately became extremely pale and cold, and neither color nor warmth returned during the fifteen minute period of occlusion. Because of this observation it was felt unwise to carry out complete ligation. Consequently, the artery was con-

stricted to about one half of its diameter with a strip of fascia which was secured with interrupted mattress sutures of silk, and by a band of cellophane about the artery. After the partial ligation the right radial pulse was smaller than the left and oscillometric studies revealed that oscillations in the right arm were reduced by about 40 per cent as compared with those in the left arm.

During the next few days the pulses and oscillations in the right upper extremity were reduced, but by the fifteenth day they were equal to those in the left. The bruit had increased in intensity after operation but was now the same as on admission. Roentgenograms revealed the aneurysm to be no smaller (Fig 2). It was felt that the band about the artery had possibly given way, at any rate there was no longer evidence that the artery was partially constricted. In view of the ischemia which had occurred during complete temporary occlusion it was decided to perform a sympathectomy in the hope that it might render the collateral circulation adequate. This was carried out on April 9. Thereafter, the right hand was warmer and better colored than the left.

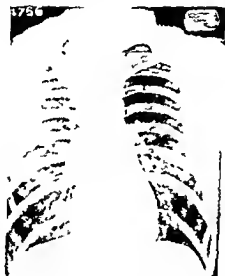


Fig 5—Roentgenograms taken eleven weeks after the final operation. the mass has disappeared.

On June 2 the mediastinum was again explored. At the initial operation the proximal artery had been readily accessible but not the subclavian which lay underneath the retracted right side of the manubrium and the sternoclavicular joint. Consequently in order to provide better exposure splitting of the sternum was supplemented by subperiosteal resection of the inner third of the right clavicle. The anterior scalene muscle was sectioned. Exposure was excellent. The aneurysm was about 10 cm long and 6 cm in diameter (Fig 3). It lay in the right side of the mediastinum and extended one centimeter above the upper border of the divided manubrium. It was lateral to the artery and was partly covered by the innominate vein. The subclavian, internal jugular and innominate veins were divided between transfixing ligatures and the intervening segment removed. There was a great deal of scarring in the vicinity of the previous partial ligation and this made isolation of the proximal artery difficult. As this was being accomplished the sac was torn just at its origin. Bleeding was effectively controlled by digital pressure while a clamp was placed across the innominate artery and the carotid and subclavian arteries were ligated between transfixing ligatures of silk. The proximal innominate artery was now ligated with umbilical tape and transfixed and ligated with silk just distal to the tape. The aneurysm was completely stilled and there was no bleeding. The sac was opened widely and a large

amount of laminated thrombus removed. A little fibrin foam was placed in the wound. The sternum was brought together with three wire sutures, the clavicular periosteal bed was closed with silk sutures as were the fascia and skin. Blood pressure had not fallen below 100 mm. during the operation. Two pints of whole blood had been administered.

Two hours after operation a nonpulsatile hematoma developed in the wound. The skin sutures were removed, the clot evacuated and since no bleeding occurred after thorough irrigation the wound was closed. There was no further bleeding.

The postoperative course was uneventful. The patient was kept in bed for approximately three weeks. There was good firmness in the region from which the clavicle had been resected, normal contour and normal movements of the shoulder (Fig. 4). There was no bruit and there were no complaints except for persistence of the slight weakness of the right upper extremity. The right hand remained warm and well colored. After a long furlough he was separated from the service early in September 1945. He still had a vocal cord paralysis but spoke well. Roentgenograms showed no mass in the area formerly occupied by the aneurysm (Fig. 5). The patient has remained well except for slight general weakness and a little fatigability of the right hand.

DISCUSSION

In Table I are listed data concerning thirty eight reported cases of attempted surgical treatment for innominate aneurysm. References to all but the last two are included in the reports of Greenough,¹ Rundle,² and Landskog.³ I have omitted one patient listed by Greenough in whom the ligation of the artery was apparently distal to the aneurysm (Cuneo) and I have included three cases (Cooper, Gay, Ballance) cited by Greenough as subclavian aneurysms which according to the operators' description apparently involved the distal portion of the innominate. Patients treated by wiring of the aneurysm, distal ligation and surgical production of an arteriovenous fistula are not included.

It is apparent that the mortality in the reported cases is very high in the patients treated some time ago and much lower in those operated upon in recent years. Excluding those cases of Matas in which the date of operation is not given, twenty operations were performed prior to 1924 with deaths in thirteen, a mortality of 65 per cent, while fifteen were done more recently with four deaths, a mortality of 26.7 per cent. Whether the mortality rate has actually been improved to this extent is open to question. It is likely that nearly all of the earlier cases may have been reported while in recent years there has perhaps been a tendency to continue to record in the literature most of the successful cases but not all of those in which a fatal outcome prevailed. Nevertheless it would appear that the mortality rate has been significantly reduced. This achievement can be attributed only in part to the fact that aseptic technique has become well established, anesthesia safer and operations made less hazardous by the use of blood transfusions. As one can easily ascertain from reading the various reports, some of the early cases were lost because of inadequate operative exposure. I believe this subject is being presented, and will not be discussed further here. Needless to say, adequate exposure is essential.

It appears that the age of the patient has not been an important factor in the mortality rate. Considering those cases in which such data are available, the average age of the patients who died in the early group was 45 years of

TABLE 1 REPORTED CASES OF DIRECT SURGICAL ATTACK UPON INNOMINATE ANEURYSMS

CASE NO	SURGEON	YR. OF OPERATION	ANEURYSM		AGE OF PT	SURGICAL PROCEDURE*	RESULT
			TYPE	LOCATION			
1	Key	1844	Spontaneous	Distal I & S	46	Attempted ligation	Died 23rd day of traumatic obstruction
2	Cooper	1859	Spontaneous	B	—	Ligation I	Died of uremia
3	Helferich	1890	Spontaneous	B	39	Attempted ligation sac torn, Jackel	Died 16th day of infection
4	Parham	1894	Spontaneous	B	45	Attempted ligation through external trephine	Died in 17 hours
5	Burrell	1895	Spontaneous	B	54	Ligation I	Recovery and relief died 104 days later of arterio-sclerotic heart disease
6	Gray	1896	Spontaneous	—	39	Ligation I, 19 days later	Died 42nd days of hemorrhage and infection
7	Gay	1896	Spontaneous	B	39	Ligation I, 32 days later	Died of secondary hemorrhage and infection on 41st day
8	Bennett	1898	Spontaneous	B	55	Ligation and division I	Died 3rd day of hemorrhage
9	Schumpert	1898	Spontaneous	B	42	Ligation I	Died 5th day of cerebral softening
10	De Laup	1900	Spontaneous	B & S	58	Ligation I	Died 18th day of secondary hemorrhage while vertebral and carotid arteries were being ligated original ligature had cut through and circulation had been re-established
11	Ballance	1902	Spontaneous	B	35	Ligation I & C	Died 2nd day with hemiplegia
12	Halsted	1907	Spontaneous	B	51	Ligation I	Recovery. On 14th day metal band placed about carotid. Unimproved until shortly before death 11 mo later
13	Kimura	1908	Spontaneous	B	46	Ligation & div I C & S. Partial excision of sac	Cure followed up 14 mo
14	Ballance	1909	Spontaneous	B	30	Sac was torn ligation I	Died in 30 hr
15	Sargent	1909	Spontaneous	Mid & distal I	67	Ligation I & C	Recovery relief died 17 mo later of pneumonia and nephritis
16	Lesnoir	1915	Traumatic	Distal I & C	—	Ligation I	Cure
17	Hamann	1916	Spontaneous	B	29	Ligation I & C	Died 4th day with hemiplegia
18	Reid	1918	Spontaneous	I involving origin	45	Died before ligation accomplished	Carotid and subclavian ligation had been performed 10 mo previously
19	Halsted	1918	Traumatic	Distal I	—	Pent in artery aneurysm after opening sac	Postoperative good result

*Abbreviations: I innominate S subclavian C carotid B bifurcation of innominate

TABLE I—CONT'D

CASE NO	SURGEON	YR OF OPERATION	ANEURYSM		AGE OF PT	SURGICAL PROCEDURE*	RESULT
			TYPE	LOCATION			
20	Ballance	1918	Spontaneous	Distal I	60	Ligation	Cure, died 2½ yr later of pulmonary infarct
21	Matas	---	Spontaneous	I	-	Metal band about I	Died on 6th day, hemorrhage and pulmonary complication
22	Matas	----	Spontaneous	I	-	Metal band about I	Recovered
23	Matas	----	Spontaneous	I	-	Metal band about I	Recovered
24	Greenough	1924	Spontaneous	Distal I	45	Ligation I, C & S	Recovery, relief, follow up 5 mo
25	Miller, Dolby, Ballance	1925	Spontaneous	Distal I & B	54	Ligation I, subsequent ligation C & S	Recurrent 8 yr later with death from rupture
26	Flint	1927	Traumatic	B	37	Ligation I trans-aneurysmal ligation S lacking	Cure, six mo follow up
27	Soutar	1933	Spontaneous	Distal I & S	62	Ligation I & S	Well
28	Lezer	1934	Traumatic arterio-venous	I	24	Transaneurysmal suture I ligation I vein	Died 17th day of infection
29	Turner	1934	Spontaneous	I	67	Attempted ligation	Died of hemorrhage on 4th day, carotid and subclavian had been ligated some years preceding operation
30	Edwards, Carling	1935 1936	Spontaneous recurrent	I I	64 -	Ligation I Ligation I, C & S sac excised	Recurrent Cure, follow up 1 yr
31	Carling	1936	Spontaneous	I	49	Ligation I, C & S	Paresis, living 2 yr later
32	Meade	1936	Spontaneous	Distal I & S	65	Ligation I & S with fascial strips	Improved pulsation persisted
33	Broek	1939	Spontaneous	I and an other of aorta	66	Ligation I	Infection and hemorrhage died 5th week
34	Langley	1943	Traumatic	Distal I	23	Ligation I, C & S	Died in 16 hr of shock hemiplegia & pulmonary edema
35	Elkin	1945	Traumatic arterio-venous	I artery both I veins	25	Ligation I, artery proximally & distally, ligation I vein distally	Cure
36	Trent	1944	Spontaneous	I involving origin	52	Rubber band partial ligation I	Clinical cure, follow up 10 mo
37	Lundskog	1945	Traumatic	Distal I	25	Ligation I prelumbar ligation C	Well
38	Shumacker	1945	Traumatic	Distal I	25	Ligation I, C & S sac evacuated	Cure, follow up 18 mo, had preliminary partial ligation with fascia & cellophane & sympathectomy

those who survived 556, in the more recent group the average age of the patients who died was 47.3 and that of those who survived about the same 46 years. To inquire further into the cause of death it will be noted that one patient is said to have died of tracheal obstruction, one of uremia, two of infection, three of cerebral ischemic difficulties, and 8 of hemorrhage or shock. Of the patients who died from hemorrhage or shock, infection played a role in the fatal outcome in three, a pulmonary complication in another, and hemiplegia and pulmonary edema in a third. In three cases the cause of death is not stated, although it appears that hemorrhage and shock were the primary factors in at least two of them. Thus the commonest difficulty has been hemorrhage at operation, or secondary hemorrhage later. It can be anticipated that adequate operative exposure, gentle dissection of the vessels, and proper use of blood transfusions may reduce the hazard of bleeding. Undoubtedly with aseptic technique, chemotherapy, and antibiotics infection should occur infrequently. The cerebral difficulties will remain a danger but can possibly be reduced to a minimum by repeated preoperative compression of the carotid until the patient can withstand such occlusion for a long period of time.

It will be noted that six of the cases of arterial aneurysm were traumatic in origin and thirty were due to either syphilis or arteriosclerosis. As might be expected the mortality was less in the traumatic cases (16.7 per cent) than in those of spontaneous aneurysm (53.3 per cent). There were two traumatic arteriovenous fistulas, one patient died, one was cured.

In analyzing the various procedures which have been employed it is noted that in five instances attempts at ligation were unsuccessful and that all five patients died. Two of three patients had previously undergone ligation of the carotid and subclavian arteries. In eleven cases the innominate artery was ligated proximally. Six of the eleven died. One who survived had a metal band placed about the carotid artery afterward but was apparently unimproved until shortly before his death, eleven months later. Four of those who survived were said to have been cured or relieved of symptoms, although in one recurrence took place early and was successfully treated later by ligation of the innominate carotid and subclavian arteries and excision of the sac. In one patient the innominate artery was divided between ligatures; he died of hemorrhage on the third day. In six patients the innominate was partly constricted proximally, three times with a metal band, once with a rubber band, once with fascia, and once with fascia and cellophane. One of the first three died and two recovered; the result in these two patients is not cited. The fourth was apparently cured following partial proximal occlusion with a rubber band. The fifth apparently had little or no effect from partial occlusion and was cured three and one half months later by ligation of the innominate carotid and subclavian arteries with opening and evacuation of the sac. Another was treated by partially constricting fascial bands about the innominate and carotid; he was improved although pulsation of the aneurysm persisted. A good result was obtained in one patient from suture of the rent in the artery after opening the sac.

Six patients were treated by ligation of the innominate and carotid arteries four died and two recovered. In one of the two successful cases the carotid artery was ligated as a preliminary measure. In two of the fatal cases the carotid was ligated after the original operation. Another patient has been previously mentioned in whom a poor result followed ligation of the innominate artery and subsequent partial occlusion of the carotid. In two cases the innominate and subclavian arteries were ligated with cure of the aneurysm. Seven patients were treated by ligation of the innominate carotid and subclavian arteries. In one of these the sac was partially removed in one it was opened and its contents evacuated and in one the sac was excised. One patient died. In five cases the aneurysm was apparently cured although a paresis occurred in one while the seventh patient had a recurrence eight years later with rupture and death. In this last case the ligation of the carotid and subclavian arteries was performed after the innominate had been ligated in the others the ligations were all done in one session. As has been mentioned two of the patients had been operated upon before one having had little or no effect from a partial innominate ligation the other having had a prompt recurrence after complete innominate ligation. There were two cases of arteriovenous fistulas. One patient was treated by proximal and distal ligation of the vessels with cure the other by transvenous suture of the artery and ligation of the vein with a fatal outcome. These data are summarized in Table II.

TABLE II ANALYSIS OF RESULTS OF VARIOUS OPERATIVE PROCEDURES

OPERATION	NUMBER OF CASES	DEATHS	CURE PROVED	IMPROVED AND CURED	RESULTS NOT STATED
<i>Arterial Aneurysms*</i>					
Attempted ligation†	5	5			
Proximal ligation	11	6	1	4‡	
Partial proximal ligation§	6	1	1	2	2
Suture of artery	1			1	
Ligation of innominate and carotid		4		2	
Ligation of innominate and subclavian	2			2	
Ligation of innominate carotid and subclavian	7	1		6	
<i>Arteriovenous Fistulas</i>					
Transvenous suture ligation of vein	1	1			
Proximal and distal ligation of artery and distal ligation of vein	1			1	

*Not counting preliminary carotid or subclavian ligations there were 38 operations upon 31 patients.

†One distal pre-lig carotid and subclavian ligation.

‡One recurrent.

§One bilateral partial carotid ligation.

¶The sac was opened and evacuated in one partially excised in one excised in one. In one case recurrence took place 8 years later with rupture and death.

In each group there are too few cases to permit a comparison of the safety and effectiveness of the various methods of treatment. It goes without saying that if the artery could be safely and securely repaired this would be the procedure of choice but it is likely that this method will be found applicable

only in rare instances. Taking into consideration the data reviewed together with experiences in the surgical treatment of peripheral aneurysms it would appear that the best procedure from the standpoint of safety to the patient and likelihood of cure of the lesion is proximal and distal ligation, combined when feasible with excision of the sac or evacuation of its thrombus. In most instances the distal ligation will involve ligation of the carotid and subclavian arteries. In these cases as in all instances of arterial surgery it will be wise when possible to divide and transect the arteries rather than to ligate in continuity. Although the matter is still controversial, it is my policy to ligate the concomitant vein when occlusion of a major artery is necessary.

I have already mentioned the danger of cerebral ischemia and its possible reduction through repeated testing of the patient's ability to withstand prolonged carotid compression. In certain instances it may be advisable to perform a preliminary ligation of the carotid artery with a removable metal band, or fascial or tape ligature. As Lindskog³ has pointed out, no case of gangrene of the upper extremity has been reported, although other evidences of ischemia have been observed not infrequently. In my patient temporary occlusion of the innominate rendered the hand pale, cold, and apparently bloodless. It would be wise to test the collateral circulation by observing the hand during temporary occlusion of the artery in every case before proceeding with permanent ligation and to employ means of increasing the efficiency of the collateral circulation when necessary.

It is of significance that all save two of the patients treated by direct surgical attack had lesions involving the mid or distal portions of the innominate artery. In one of these the patient died before ligation could be accomplished. Only in the case of Trent was the outcome successful when the lesion involved the origin of the vessel.⁴ Although the result in Trent's patient was excellent in general, when the first portion of the innominate artery has been affected such procedures as ligation have not been found practicable. I know of no other successful case but several unreported fatalities following attempt at such treatment have come to my attention. Unless the rubber band constriction which Trent used should prove the answer to this problem and the experience with its use in aneurysms of the aorta would suggest that it may sometimes end in disaster, some other more indirect effort to control the aneurysm must be adopted in such cases. Thus far I have not mentioned such measures as Babcock's surgical production of a carotid jugular arteriovenous fistula,^{5,6} distal ligation of the carotid and subclavian arteries employing the principle

the aneurysms. Matas⁷ has commented upon Babcock procedure and upon the functional difficulty of not believing it has a place in the surgical

treatment of innominate aneurysms. Although some excellent results have been reported with the technique of Brasdor Guinard^{8,9} and though it may be applicable in rare cases, it would appear to be associated with definite risk and with only a moderate chance of relief of symptoms. In cases in which direct surgical attack has not proved feasible, I have felt that wiring and coagulation is the procedure of choice. I have used this method as developed by Blakemore and

King in several cases in which the aneurysm involved the origin of the innominate. This procedure often brings about arrest of expansion of the aneurysm and relief of symptoms although it cannot be considered a curative measure. It is entirely possible that a combination of wiring and coagulation with distal ligation of the carotid and subclavian arteries may yield better results than wiring and coagulation alone. Once the sac wall has been reinforced by an increase in the intramural thrombus following this procedure there should be little hazard associated with distal ligation while after distal ligation there should be a good possibility of obtaining complete saccular thrombosis with further wiring—an accomplishment practically impossible with wiring alone. This plan at least deserves trial and it is my intention to test its worth when the opportunity presents itself.

SUMMARY AND CONCLUSIONS

A case of surgical cure of an innominate aneurysm has been reported and the literature has been briefly reviewed. It appears that direct surgical attack upon innominate aneurysms will necessarily be largely limited to those cases in which the origin of the artery is not involved. The best procedure which will ordinarily be found to be applicable in these cases would seem to be proximal and distal ligation combined with excision of the sac if possible or evacuation of its contents. For those cases involving the origin of the innominate wiring and coagulation possibly combined with distal ligation is probably the safest procedure offering the likelihood of a satisfactory result.

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THE USE OF TETRAETHYLAMMONIUM CHLORIDE IN THE TREATMENT OF EXPERIMENTAL ACUTE ARTERIAL INSUFFICIENCY

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IN THE treatment of acute arterial injuries of the major vessels attention is immediately directed toward two objectives: controlling hemorrhage and overcoming the resultant acute arterial insufficiency to the tissues normally supplied by the artery and its branches.

The circulation is normally reestablished by means of collateral circulation in which pre-existing channels undergo dilatation and establish an alternate shunt around the site of injury. This restoration of blood flow may or may not be adequate depending upon the vessel involved and the level of interruption. The arterial insufficiency may be manifest by coolness, trophic changes, decreased functional tolerance, ulceration and gangrene. Therapy in most instances must be directed toward augmentation of the secondary or collateral circulation.

Numerous authors¹⁻¹³ have pointed out that inadequacy of the collateral circulation notwithstanding injury to these vessels is frequently due to an element of vasospasm which acts to diminish the caliber of these vessels. This active vasomotor tone is the direct result of an outflow of vasopressor impulses from an intact sympathetic nervous system. The normal tone maintained in health is further increased by reflex spasm resulting from the proximate arterial injury. It has been demonstrated clinically and experimentally¹⁴⁻¹⁸ that interruption of this sympathetic outflow by various methods results in an increased blood flow through collateral channels as evidenced by a rise in skin and deep temperatures, decreased venous filling time, increased oscillometric readings, and the prevention of tissue death.

Leriche and Stricker and Orban in a series of experiments² proved conclusively the value of sympathectomy in the prevention of massive gangrene and death following extensive arterial resection in animals. They found that following resection of the terminal aorta and its branches in the lower more than four fifths of their animals died in twenty-four hours to four days with paralyzed cold cyanotic and edematous hind limbs. If however bilateral lumbar sympathectomy was performed at the same time just prior to the arterial resection the animals showed little ill effects. Within twenty-four hours they could stand and walk with warm hind limbs and little evidence of circulatory insufficiency. At the end of a week they were as active as normal animals.

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Reichert¹⁴ has excellently demonstrated the collateral channels which enlarge following ligation of the aorta in dogs by the injection of a roentgenographically opaque mass. He has stated that the abdominal aorta can be ligated without danger of gangrene.

Brooks¹ has shown that following experimental ligation of the abdominal aorta below the inferior mesenteric artery and without excision and division there is always definite evidence of impairment of circulation. In most instances he reported evidence of impaired function and in a few instances gangrene of the feet. A considerable number of his animals died after ligation of the aorta without any known cause.

Recently reports have appeared concerning the pharmacologic action of the tetraethylammonium ion upon the sympathetic nervous system. This drug acts chiefly to block at the autonomic ganglia the transmission of sympathetic and parasympathetic nerve impulses. The pharmacology has been reviewed in detail by Acheson and Moe.¹⁵ Proof was afforded that the chief if not the sole locus of action of tetraethylammonium ion is at the autonomic ganglia. The intravenous administration of vasodepressor doses of the drug causes an increase in blood flow through the femoral artery.

The following series of experiments was undertaken to determine the efficiency of chemical sympathetic blockade in experimental acute arterial injuries. No attempt has been made to compare results of treatment with the tetraethylammonium ion with other methods of sympathetic interruption.

EXPERIMENTAL METHOD

Since the result of aortic ligation alone is variable as to survival of the animal or gangrene of the posterior extremities and since various authors have reported varying percentages of deaths following excision of the trifurcation of the aorta in this series a more extensive resection was carried out. The operation was extended to include the deep circumflex iliac vessels which constitute one of the major collateral channels following aortic ligation. If these vessels had their origin above the inferior mesenteric artery they were ligated and divided at that point. In this manner the arterial supply to the extremities was reduced to a critical level.

A group of thirty adult mongrel dogs weighing from 9 to 15 kilograms was selected. Identical operative procedures were carried out on all animals in the group. Surgical anesthesia was obtained by the intravenous administration of sodium pentobarbital (64 mg. per five pounds body weight). Under aseptic precautions the aortic trifurcation was exposed. The terminal aorta was doubly ligated distal to the origin of the inferior mesenteric artery but proximal to the origin of the deep circumflex iliac arteries. Ligatures were placed around the two external iliac arteries and the common hypogastric trunk. The intervening aortic trunks were excised. The abdominal wound was closed in layers.

In the control group of ten dogs nothing further was done; the animals being closely observed until the time of their death following which autopsy was performed.

In the experimental group administration of tetraethylammonium chloride* was begun immediately after excision of the arteries. This was given in the proportion of 25 mg per kilogram body weight, as a sterile 10 per cent



Chart I—Results of aortic excision in untreated animals

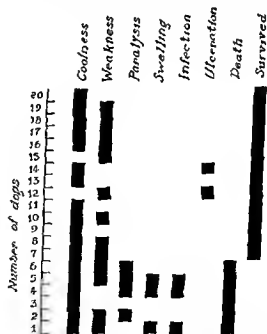


Chart II—Results of aortic excision in animals treated with tetraethylammonium chloride

*Supplied as Etamon by the Parke Davis & Company Detroit Mich

solution intramuscularly. Similar doses were given every eight hours for three days.

All the animals were allowed food water as desired and offered exercise at least once daily, as tolerated.

RESULTS

In the control group nine of the animals died within twenty four hours to seven days. The majority of deaths were within a four day period. Autopsy revealed in each instance that death was not due to hemorrhage from the ligated arteries or to peritoneal infection. Prior to their death these animals exhibited the same findings as reported by Leriche: hindlimb paralysis, coldness, cyanosis and varying degrees of swelling.



Fig. 1—A. Arteriogram immediately following ligation of the terminal aorta, little filling of the collateral vessels occurs. B. Arteriogram following injection of thorotrast into the aorta of a normal dog.

In the group of twenty animals treated with tetraethylammonium chloride fourteen of the animals survived. These animals regained excellent functional activity within two to six days. Of the remaining six dogs which died three deaths were the result of infection of a posterior extremity. One of the remaining animals died within twelve hours of operation and the other on the tenth postoperative day from an undetermined cause.

Arteriograms were performed immediately following ligation and excision of the aorta in control animals (Fig. 1 B). In such instances there was little filling of the collateral channels by the contrast media. In the animals which survived following tetraethylammonium chloride therapy a graded increase in filling of the vessels could be roentgenologically demonstrated (Figs. 2 and 3).

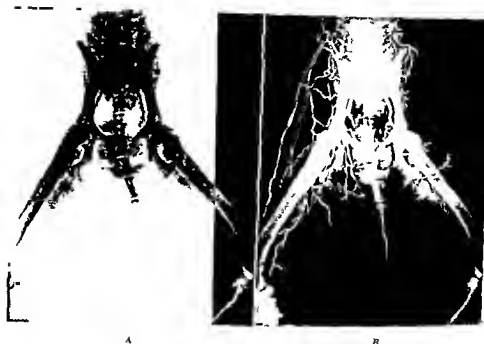


Fig 2—A Arteriogram seven days following excision of the trifurcation of the aorta and postoperative treatment with tetrathylammonium chloride. The deep circumflex iliac vessels are filled as are the internal iliac. B Retouched roentgenogram.



Fig 3—A Arteriogram fourteen days following aortic excision and tetrathylammonium chloride therapy. The femoral vessels fill readily. B Retouched roentgenogram.

DISCUSSION

The results obtained from chemical blockage of autonomic ganglia are thought to be due to a removal of vasomotor constriction of collateral vessels thus permitting their dilatation. In these experiments the immediate time interval following arterial resection referred to by Leriche as the critical period appears to be the optimum time for removal of vasomotor constrictor impulses. Once an increased collateral circulation is established it is able to maintain itself and probably undergoes a graded increase over later intervals as evidenced by the increased tolerance for daily exercise.

In view of these experimental results it is suggested that tetraethylammonium chloride may become a valuable adjunct in the clinical treatment of acute arterial injuries involving major vessels.

SUMMARY

1 The rationale for sympathetic interruption following acute arterial injury is presented.

2 Experimental observations have been made which indicate that chemical blockage of autonomic ganglia by tetraethylammonium ion may be of value in acute arterial insufficiency following arterial injury both as a substitute for other methods of sympathetic interruption or as a preliminary to them.

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THE ACTION OF HEPARIN ON EXPERIMENTAL VENOUS THROMBOSIS

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THE extensive clinical trial of heparin, both here and abroad in the prophylaxis and treatment of venous thrombosis has stimulated our interest in those properties of heparin which relate directly to this problem. The purpose of this paper will be to elaborate upon the *in vivo* action of heparin on the preformed clot.

The possibility that heparin might prevent vascular thrombosis was first enunciated by Howell.¹ Mason² in 1924 showed that heparin will prevent the formation of an intravascular clot induced by the injection of potent thrombokinase into the blood stream. Experimental evidence indicating that heparin will protect against the intravascular thrombosis which ordinarily would occur after traumatic and mechanical means has been reported by Murray and his co-workers,³ Best, Cowan, and MacLenn⁴ and by Rabinovitch and Pines.⁵ There is, however, a considerable variation of opinion as to the effect of heparin on the preformed clot. This may be ascribed to the different methods of inducing thrombosis, to the varying strengths of heparin used and, finally to the modes of administration of this agent. It would be fitting at this point to review the major experimental work on this most controversial subject.

The acknowledged failure of heparin to act on the *in vitro* clot is readily demonstrable and has recently been reaffirmed by Rabinovitch and Pines. However the *in vivo* clot has on occasion been seen to disappear. This startling contrast between *in vivo* and *in vitro* action has stimulated many observers to determine if possible the precise action of heparin in the living organism since the *in vivo* anticoagulant property of heparin is fraught with therapeutic possibilities. In a series of experiments inaugurated in 1932 and reported in 1937 by Murray, Jaques Perrett and Best,³ thrombosis was initiated in veins of dogs by either mechanical or chemical trauma. The mechanical trauma was accomplished by crushing a vein over an intraluminal silk thread with a hemostat following which the thread was removed and the wound sutured. Occluding thrombi appeared in seven hours to seven days in 80 per cent of the cases. Chemical trauma was effected by the introduction and retention of sorcin in the vein for three minutes. By this method 65 per cent of the veins were thrombosed. Heparin was given for varying periods before and after trauma. Trauma following prophylactic heparin administration resulted in a few minimal thromboses, the majority of veins remaining

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patent if additional heparin was given subsequently. Heparin given after trauma maintained the patency of a number of veins, the percentage of patent vessels being inversely proportional to the length of time ensuing between trauma and inception of heparin therapy.

To summarize all the recorded experiments 14 per cent of the control veins were patent after mechanical trauma while 81 per cent of the test veins were patent when heparin was administered for seventy to seventy-two hours. Similarly with chemical trauma 15 per cent of the controls were patent while patency was maintained in 53 per cent of the heparinized veins.

The experimental evidence that heparin did have some effect on the preformed clot was further bolstered by the results of Solandt and Best⁶ who showed that coronary thrombosis could be induced by sorjcin in twelve of thirteen control dogs while similar lesions occurred in only one of twelve dogs if heparin was given continuously for twenty-four hours after injury. Further evidence was brought forth by Rabinovitch and Pines⁷ whose method of inducing thrombosis consisted of stretching the vein thus causing endothelial damage. A constricting silk ligature was then used to occlude the lumen partly. Heparin was subsequently administered in bidaily intravenous doses for five or six days. These investigators showed that in certain instances heparin caused the disappearance of the thrombus only in the early stages and never when the clot had already been organized.

To recapitulate: (1) If heparin was given previous to trauma and continued for a variable period afterward thromboses were infrequently observed. (2) Heparin administered up to three days after trauma caused disappearance of the clot in a considerable percentage of cases. (3) Heparin administered when the clot was organized resulted in no demonstrable dissolution of the clot.

It occurred to us to determine if possible at what stage of clot formation heparin administration would result in solution of the clot and what effect if any heparin had on the organizing clot.

METHODS

Induction of Thrombosis.—Experimental venous thrombosis has hitherto been accomplished by chemical and mechanical means. Although Murray and his co-workers reported 80 to 85 per cent successful thromboses with their methods, the 15 to 20 per cent margin of error seemed too great for critical evaluation. Similarly in our hands stretching the vein by the method of Rabinovitch and Pines was not successful in the majority of cases. It is obvious from both the experimental work on thrombosis and the theoretical considerations of blood coagulation that the elaboration of a successful thrombus depends on (a) stagnation of blood, (b) injury to the intima, (c) release of considerable amounts of thrombokinase from the vessel walls. After numerous trials a method of experimental induction of thrombosis was devised which fulfills all the requirements set forth previously and which is uniformly successful. Three kilogram rabbits are anesthetized with ether and a midline cervical incision is made. The jugular veins on either side are exposed both

THE ACTION OF HEPARIN ON EXPERIMENTAL VENOUS THROMBOSIS

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THE extensive clinical trial of heparin both here and abroad in the prophylaxis and treatment of venous thrombosis has stimulated our interest in those properties of heparin which relate directly to this problem. The purpose of this paper will be to elaborate upon the *in vivo* action of heparin on the preformed clot.

The possibility that heparin might prevent vascular thrombosis was first enunciated by Howell¹ & Mason² in 1924, who showed that heparin will prevent the formation of an intravascular clot induced by the injection of potent thrombokinase into the blood stream. Experimental evidence indicating that heparin will protect against the intravascular thrombosis which ordinarily would occur after traumatic and mechanical means has been reported by Murray and his co-workers,³ Best, Cowan and MacLean,⁴ and by Rabinovitch and Pines.⁵ There is, however, a considerable variation of opinion as to the effect of heparin on the preformed clot. This may be ascribed to the different methods of inducing thrombosis, to the varying strengths of heparin used, and finally to the modes of administration of this agent. It would be fitting at this point to review the major experimental work on this most controversial subject.

The acknowledged failure of heparin to act on the *in vitro* clot is readily demonstrable and has recently been reaffirmed by Rabinovitch and Pines.⁵ However, the *in vivo* clot has on occasion been seen to disappear. This startling contrast between *in vivo* and *in vitro* action has stimulated many observers to determine, if possible, the precise action of heparin in the living organism since the *in vivo* anticoagulant property of heparin is fraught with therapeutic possibilities. In a series of experiments inaugurated in 1932 and reported in 1937 by Murray, Jaques, Perrett and Best,³ thrombosis was induced in veins of dogs by either mechanical or chemical trauma. The mechanical trauma was accomplished by crushing a vein over an intraluminal silk thread with a hemostat, following which the thread was removed and the wound sutured. Occluding thrombi appeared in seven hours to seven days in 80 per cent of the cases. Chemical trauma was effected by the introduction and retention of soricin in the vein for three minutes. By this method 85 per cent of the veins were thrombosed. Heparin was given for varying periods before and after trauma. Trauma following prophylactic heparin administration resulted in a few minimal thromboses, the majority of veins remaining

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TABLE I THE ACTION OF HEPARIN ON THE PRE FORMED CLOT IN THE RABBIT

HEPARIN						CONTROL				
DAYS AFTER TRAUMA AND BEFORE HEPARIN THERAPY	NUM BER OF VEINS	PERIOD OF THERAPY	PATENT	OCCLUDED	COL LATER ALS	DAYS AFTER TRAUMA AND BEFORE HEPARIN THERAPY	NUM BER OF VEINS	PATENT	OCCLUDED	COL LATER ALS
1	5	6	4	1	0	1	2	0	2	0
2	3	6	2	1	0	2	3	0	3	0
3	3	13	3	0	0	3	5	0	5	0
	1	6	0	1	0					
5	3	13	2	1	0	5	4	0	4	0
6	1	6	0	1	1	6	4	0	4	0
	2	13	1	1	1 2					
7	4	13	3	1	2					
8	3	13	0	3 (partly)	2	8	1	0	1	0
9	4	13	0	4 (partly)	3	9	4	0	4	0 1
10	1	13	0	1 (partly)	2 3	10	5	0	5	0 1
11	1	14	0	1 (partly)	3	11	2	0	2	1
	1	6	0	1	2					
13	3	14	0	3 (partly)	3	13	2	0	2	1
14	9	14	0	9	4	14	2	0	2	1
						15	1	0	1	1
						24	10	0	10	1 2
44						45				

TABLE II

DAYS (INCLUSIVE) AFTER TRAUMA AND BEFORE HEPARIN THERAPY	DAYS OF HEPARIN	NUMBER OF VEINS	PATENT	OCCLUDED	COLLATERALS
15	6	9	6	3	0
	13	5	5	1	0

TABLE III

DAYS (INCLUSIVE) AFTER TRAUMA AND BEFORE HEPARIN THERAPY	DAYS OF HEPARIN	NUMBER OF VEINS	PATENT	OCCLUDED	COLLATERALS
6 "	6	1	0	1	1 plus
	17	6	4	2	1 plus

TABLE IV

DAYS (INCLUSIVE) AFTER TRAUMA AND BEFORE HEPARIN THERAPY	DAYS OF HEPARIN	NUMBER OF VEINS	PATENT	OCCLUDED	COLLATERALS
8 13	6	1	0	1	2 plus
	13	1	0	12 partly	2 plus and 1 plus

veins being treated alike. A 3 cm segment of vein is dissected free and the most proximal portion is securely tied with a silk ligature. A flat narrow strip of metal, such as a ribbon retractor* is placed under the vein distal to the ligature and acts as an anvil. The vein is then given fifteen to thirty sharp taps with the handle of a Mayo scissors. Brisk bleeding will occur which is readily controlled by gauze pressure. Care is taken not to fracture the vein completely across. When bleeding has ceased usually in about two minutes a palpable and visible clot appears. If this does not occur the procedure is again repeated. Clotting invariably is present after the second series of strokes. All animals are re-examined after forty eight hours to reaffirm the presence of clots.

Heparinization—The method of continuous heparinization as reported by Murray and his co-workers is obviously impractical in animals if heparinization is to be continued for long periods of time. Similarly intermittent heparinization is not consistently effective in that the coagulation time may well fall to normal levels in the interval between successive doses of heparin. As a matter of fact the coagulation time may undergo a biphasic reaction and induce a state of hypercoagulability. Because of these objections we were constrained to use the heparin/Pitkin menstruum preparation†. The Pitkin menstruum is a gelatin base medium which was designed to regulate and retard the release of water soluble drugs incorporated within it. The preparation with varying amounts of heparin has been extensively used on human patients with uniformly excellent results^{9, 10, 11}. The formulas employed in our experiments contained vasoconstrictors which further delayed the absorption of the heparin and prolonged the effect of a single dose. The dosage has varied from 40 to 100 mg. of heparin given every two to three days. The amount was governed solely by the coagulation time which was maintained at two to four times the normal level. Coagulograms were determined by a modification of the Lee White method which has been completely described elsewhere¹⁰. No hemorrhages were encountered in our series.

EXPERIMENTAL RESULTS

From Table I the scope of the experiment is evident. Thrombosis was induced in both jugular veins of 3 kg. rabbits by the method described. In all instances except the one day animals the veins were examined after forty eight hours to determine the presence or absence of thrombosis. In our earlier work absence of clot was noted on occasion so that thrombosis had to be re-induced. With improvement in our techniques as evidenced by the last 99 veins reported in Table I no failures were encountered. At variable periods after the induction of thrombosis if the forty eight hour re-examination proved to be satisfactory the wound was opened and the left jugular vein removed for control microscopic section. The animal was then heparinized for six to fourteen days after which the wound was again opened, the lesion photographed and the remaining jugular vein removed for microscopic study.

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†Prepared and distributed by William R. Warner & Co., Inc., New York, N. Y.

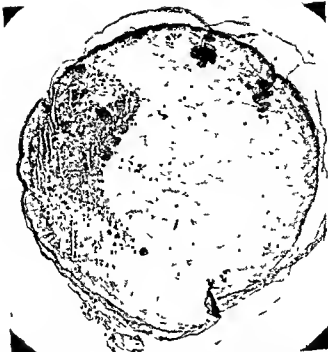


Fig 2 (Rabbit 82) —Two day control the lumen is distended and is filled with an early thrombus. The wall is thin and the elastic tissue is still fairly well preserved (Elastic Van Gieson X21)



Fig 3 (Rabbit 7011) —Six day animal with twelve days of heparin. The lumen does not contain thrombi. The internal elastic is fragmented. (Elastic Van Gieson X135)

For the purposes of analysis it is convenient to subdivide Table I into four sections, these subdivisions (Table II, III, IV, and V) relate to the heparinized animals and indicate the number of days from inception of trauma to the initiation of heparinization. Table II included the first through the fifth days, Table III the sixth through the seventh, Table IV the eighth through the thirteenth, and Table V included all of the fourteen day animals.

From Table II (one to five days after trauma and before heparinization) it is evident that of nine veins with but six days of active heparinization, six were patent and three were occluded. Of six veins with thirteen days of heparinization, five were patent (Fig 1) and one was occluded. No collaterals were observed. In the control nonheparinized group of fourteen veins, all fourteen were occluded (Fig 2).



Fig 1 (Rabbit 86H)—Two day animal with eleven days of heparin. The lumen is empty. The wall is thin and the elastic tissue is well preserved (Elastic Van Gieson X70).

Table III (six to seven days after trauma and before heparinization) reveals that of six veins heparinized for thirteen days, four were patent (Fig 3) and two were occluded. Small, single collaterals were seen to parallel the heparinized vein, while none were seen accompanying the nonheparinized controls. All six of the control veins were occluded (Fig 4).

Table IV (eight to thirteen days after trauma and before heparinization) was of considerable interest to us in that all the twelve veins which had been heparinized for thirteen days appeared clinically patent. The veins were thickened but blue and somewhat collapsible so that blood flow through these vessels was clinically obvious. However, on microscopic section these presented various degrees of organization and recanalization (Figs 5 and 6). One vein, examined after six days of heparinization appeared to be a solid cord. All of the fourteen control veins were thickened, gray noncollapsible structures which, on microscopic section, were seen to be organized with

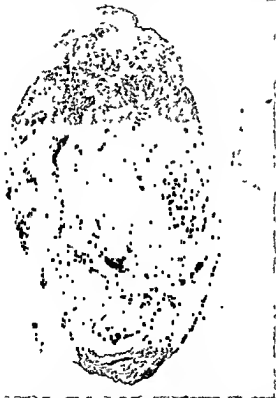


Fig 6 (Rabbit 6111) —Nine day animal with thirteen days of heparin. The lumen contains a thrombus which is undergoing organization and recanalization. The elastic tissue is fragmented and reduplicated. (Elastic Van Gieson $\times 60$)

evidence of recanalization (Fig 7). The extent of recanalization and the diameters of the recanalized lumina appeared greatest in the animals heparinized for thirteen days. The heparinized veins were accompanied by two to three fairly large collateral vessels while the control veins of comparable age had one or, at most, two tiny to medium sized collaterals.

Table V (fourteen days after trauma and before heparinization) represents nine veins heparinized for fourteen days. All of these were identified only by the encircling black silk ligature. The veins were gray, solid, threadlike struc-



Fig 4 (Rabbit 70) — 0-day control the lumen is filled with a thrombus. The elastic tissue is fragmented and the various coats of the vessel wall are poorly differentiated (Elastic Van Gieson X40)



Fig 5 (Rabbit 63H) — 14-day animal with fourteen days of heparin. The lumen is narrow but empty. The intimal connective tissue is increased in amount. The elastic tissue is fragmented and reduplicated in places but appears to encircle the lumen. (Elastic Van Gieson X41)



Fig. 9

Fig. 9 (Rabbit vein)—A section of a rabbit vein with fourteen days of heparin. The lumen is narrow and empty. The internal elastic lamina is well defined although fragmented in places. The subintimal connective tissue is greatly increased in amount (H&E, Van Gieson X200).

Fig. 10 (Rabbit vein)—Twenty-eight days of heparin. The lumen is greatly narrowed and the vessel wall is poorly defined. The elastic lamina is fragmented. The lumen is occluded by an organized thrombus in which recanalized channels of varying size are present (H&E, Van Gieson X200).



Fig. 10



Fig. 7

Fig. 7. (Gallbladder) — Ten day exposed animal. The intima is thin and clear in places (a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, y, z). The media is thick and contains many elastic fibers (a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, y, z). The adventitia is thin and contains many elastic fibers (a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, y, z).

Fig. 8

Fig. 8. (Gallbladder) — Ten day exposed animal. The intima is thin and clear in places (a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, y, z). The media is thick and contains many elastic fibers (a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, y, z). The adventitia is thin and contains many elastic fibers (a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q, r, s, t, u, v, w, x, y, z).

TABLE V

DAYS (INCLUSIVE) AFTER TRAUMA AND BEFORE HEPARIN THERAPY	DAYS OF HEPARIN	NUMBER OF VEINS	PATENT	OCCCLUDED	COLLATERALS
14	14	9	0	9	4 plus

the restraining ligature. The control collaterals usually numbered one or two were for the most part small (in comparison to the heparinized mates) and did not form the rich anastomotic network seen in the previous group.

DISCUSSION

Several facts are immediately apparent from a study of Tables I to V. First patency can be re established in a number of experimental veins even as long as six days after a clinically visible and microscopically acceptable thrombus is present. Second the extent and apparently the speed of recanalization is enhanced by the use of heparin. Third when the vein is so occluded grossly as to preclude the resumption of clinical patency recanalization is still greater in degree and extent under heparin therapy. Fourth in the presence of occluded veins which cause definite obstruction to circulation the opening of adjacent collateral venous channels is so extensive in the presence of heparin that the combined cross sectional area of the collateral system appears as great if not greater, than that of the original vein.

These results are at variance with the published data of Murray and associates¹ and Rabinovitch and Pines. The former group administered heparin for seventy two hours after trauma while the latter in one series heparinized their animals for periods up to eight days. It is evident from our series that even eight days is too brief a period in which to extract the maximum benefit to be derived from heparin. Our fourteen day period was arrived at after extensive experience with the heparin/Pitkin menstruum preparation in patients with thrombophlebitis and/or phlebothrombosis. Assuming the seventy two hour period to be too brief beyond question the failure of the eight day period of Rabinovitch and Pines can be partly explained first by the fact that per se eight days has been shown to represent too brief a span of heparinization second the heparin as used by them yielded a good anticoagulant effect for only five hours. Since their results were predicated on a bi-daily schedule of heparin administration there obviously must have been gaps in the treatment day when the coagulation time was at normal levels or indeed as we have seen repeatedly, the level may have fallen below normal thus inducing a state of hypercoagulability. Coagulograms utilizing heparin/Pitkin menstruum reveal that maximum effects are obtained in four hours and are continued for forty eight or more hours (Graph 1). Reinjection every forty eight hours obviously will consistently maintain the coagulation time well above normal limits.

Since it is well known that heparin *in vitro* has no effect on fibrin, it appears difficult to explain the dissolution of clots up to and including the sixth day after thrombus formation. Examination of our sections demonstrates

tures which clinically seemed incapable of transporting blood. On section, these were well organized and contained large recanalized lumina (Figs 8 and 9) and not the honeycombed pattern of recanalization so evident in the control mates of comparable interval after trauma (Fig 10). Most interesting in this group were the collateral veins (Fig 11). In the heparinized series the collateral vessels were three to four in number, many as large as the original vein. Most often they formed a complex anastomosis with vessels proximal to



Fig 11 (Rabbit 5041)—Collateral vein of urethra in rabbit with fourteen days of heparin. A
the characteristics of a normal vein can be seen. (Flaugh and Gleason $\times 250$)

thrombosed veins which, on microscopic examination, reveal no evidence of clot formation in the usual sense (Figs 7 and 12). It is not surprising, therefore, that these clotted veins in the sludge stage may well be mistaken for normal red cell-containing veins. In the progressive growth of a clot, sludge formation is ever present, both as the propagating tail and as part of the unorganized body of the clot. It is significant that in every instance where pure sludge formation was noted microscopically, despite clinically palpable clot formation, the clot disappeared completely under heparin therapy.



Fig. 12 (Rabbit 79).—Three day control animal. The lumen is filled with a recent thrombus in which the lamination of the accepted early thrombus is not yet present. The blood cells are seen as individual members and have not as yet lost their identity. Here and there evidence of beginning organization is seen. (Elastic Van Gieson X24.)

Any attempt to explain the apparent dissolution of the early fibrin clot and the rapid recanalization of the late clot under heparin influence must necessarily be speculative. Further studies are in progress in an effort to clarify these moot points. The present day tendency has been to consider the mechanism of

EXTENSIVE BLUE NEVUS OF JADASSOHN-TIECHE

REPORT OF CASE

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SINCE the first blue nevus was described by Tieche,¹ there have been many reports of this lesion. According to Montgomery and Kahler² and Ormsby and Montgomery,³ review of the literature revealed that the great preponderance of blue nevi are small in size, that is, they are seldom more than 15 mm in diameter. However, more extensive blue nevi occasionally are seen. Pick and Livingston⁴ reported a case in which the back of the patient was covered by a congenital blue nevus. This patient also had von Recklinghausen's disease and a malignant melanoma subsequently developed in the interscapular area and metastasized to the lungs and brain.

We recently have observed a case of an unusually extensive blue nevus which we wish to report.

REPORT OF CASE

A white boy aged 9 years was first seen at the Mayo Clinic on May 1, 1946. His family and medical history, aside from the presenting complaint, was negative. His mother stated that she had noted a slightly raised bluish skin lesion on the left side of the child's thorax when he was 4 weeks of age. The color and size of the lesion had remained relatively unchanged during his development and no treatment had been used for the lesion. The involved area was asymptomatic.

On physical examination of the boy the salient findings were limited to the skin of the anterior and upper part of the left side of the thorax (Fig 1). Here there was an irregularly shaped lesion 3 to 6 cm in width which extended from the lower part of the sternum laterally to the left midaxillary line. The lesion was composed of multiple, firm, dark blue, round nodules which were slightly raised above the surrounding skin. There also was a bluish discoloration of the skin in intervening small areas between the circumscribed nodules. The regional lymph nodes were not palpable.

Biopsy was not performed but it was believed that the lesion was a vascular nevus because of its large size and general appearance. Excision of the lesion was advised because of its site and susceptibility to trauma.

On July 13, 1946, the involved skin and subcutaneous tissue were excised by a long elliptical incision extending from the sternum laterally to the left midaxillary line, beyond the edges of the lesion. It was then found that the fascia and lower portion of the pectoral muscle were deeply pigmented and on section the pigmentation seemed to extend through the deeper layers of muscle. The incision was not carried down to the periosteum or pleura so we do not know how deeply the pigmentation extended. The pigmented fascia and muscle were not excised. The edges of the skin were undermined, brought together and sutured, and a Penrose drain was inserted. The lesion was healing satisfactorily when the patient was dismissed on July 26, 1946.

Pathologic Examination.—The surgical specimen consisted of skin and subcutaneous tissue and measured 17 cm in length, 6 cm in width and 2 cm in thickness. Multiple,

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coagulation and the inhibition of coagulation as a physiochemical reaction.¹⁷ In any equation of this type, the basic factors consist of the types of materials entering into the reaction, the relative amount of the reacting components, the pH, and, finally, the time factor. Since every biochemical reaction is theoretically reversible, it is quite conceivable that with an increase in the amount of functioning circulating heparin which is allowed to act for a long period a reversal of the thrombin + fibrinogen \rightarrow fibrin equation may possibly occur.

Conceivably, a contributing factor in stimulating reparative processes such as organization and recanalization is the demonstrable effectiveness of heparin in enhancing and maintaining an elaborate collateral circulation. It is generally conceded that the phenomenon of recanalization is to a large extent predicated on physical factors. It is evident that the larger column of fluid blood resulting from heparinization, pounding against small recanalizing channels may well be responsible for accelerating and augmenting recanalization.

CONCLUSIONS

Heparin therapy in experimental venous thrombosis in rabbits results in the following:

- 1 Early clots are completely resolved
- 2 Growth of the collateral venous circulation is tremendously enhanced
- 3 Speed of recanalization after occlusive thrombus formation is accelerated

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positive dopa reaction when situated in the upper part of the cutis adjacent to the epidermis but it rarely retains these properties when found deep in the cutis as in the subdermal type of nevus. The cells of the blue nevus however represent true dermal melanoblasts and are laden with melanin and give a positive dopa reaction.

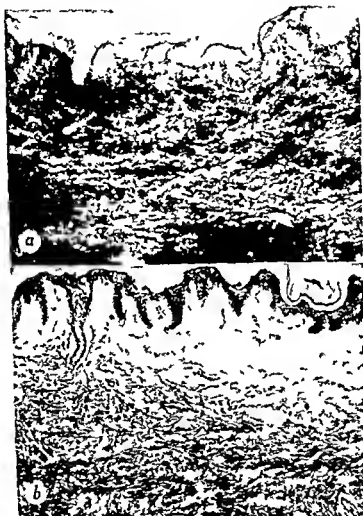


Fig. 2—*a*: Dense black masses in the lower portion of the cutis composed of dopa positive melanoblasts of the blue nevus; di-ox-phenylalanine (dopa) stain ($\times 70$); *b*: melanin pigment in basal cells at the tips of the rete ridges in the epidermis and also with a blue nevus cells in the middle and lower cutis; silver nitrate and hematoxylin stain ($\times 70$).

SUMMARY

We have observed a case in which an extensive blue nevus of Jadassohn-Tiche occurred in a white boy aged 9 years. The lesion was 17 cm in length and 3 to 6 cm in width and extended from the lower part of the sternum laterally to the left maxillary line. It was first noted when the child was

firm, dark blue nodules, which varied in size from that of a match head to that of a split pea, projected at narrow intervals from the surface of the skin throughout the extent of the lesion. On cross section, the specimen showed very dense, dark blue pigment arranged in layers. The epidermis appeared white, and beneath it the cutis was entirely blue black in color. The fat of the subcutaneous tissues was yellow with narrow streaks of the pigment growing through it at narrow intervals down into the fascia which also showed a mottled bluish pigmentation.



Fig. 1—Extensive blue nevus involving the upper left portion of the anterior wall of the thorax.

Sections stained with hematoxylin and eosin showed slight hyperkeratosis and irregular, mild proliferation of the rete ridges of the epidermis. The melanin pigment in the basal cells appeared to be increased in amount in the rete ridges. The papillary portion of the cutis appeared unchanged but in the subpapillary, middle and lower parts of the cutis, and in the subcutaneous tissues as deep as the section extended, there were multiple, irregularly nodular collections of long slender, spindle shaped cells which were concentrated about the dermal appendages of the section. These cells in frozen section, stained dark brown with dioxyphenylalanine (dopa reagent) and were dopa positive melanoblasts (Figs 2, a and 3, a). Other melanin bearing cells, which were larger, shorter and plump, and which contained coarse granules or clumps of pigment, were seen frequently. These cells were chromatophores and were seen in the upper part of the cutis above, as well as among, the masses of melanoblasts in the middle and lower parts of the cutis. The chromatophores although they contained melanin were not stained by dopa reagent and were thus dopa negative.

All of the melanin was more distinct in sections stained with silver nitrate and hematoxylin. The black melanin pigment in the cytoplasm of the basal cells of the epidermis appeared clearly, the coarse melanin pigment in the chromatophores was pronounced and the fine melanin granules distinctly outlined the long dendritic processes of the melanoblasts (Figs 2, b and 3, b, and c). This staining method revealed melanin pigment in cells which appeared nonpigmented when stained with hematoxylin and eosin and with the dopa stain.

Ordinary pigmented nevus cells were not seen in any of the sections. These cells are oval in shape, have large vesicular nuclei and are larger than the cells of blue nevus which are also characterized by their long bipolar dendritic processes. Ordinary nevus cells characteristically grow in alveoli nests or columns in contrast to the irregular strands and solid masses of blue nevus cells. The common nevus cell usually contains melanin pigment and gives a

We are able to find reports of only ten cases of malignant change in blue nevi in the literature. Histologic studies of these lesions usually reveal the presence of another type of tumor cell in addition to the blue nevus cell either in the primary lesion or the metastatic lesions. In several instances, no histologic evidence of malignant change has been present. In only one case was there clear cut pathologic evidence that a melanosarcoma had developed from a blue nevus. We believe, therefore, that this lesion is fundamentally benign and that no further treatment of the residual blue nevus was indicated in the case which we have reported.

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4 weeks of age, and remained relatively unchanged during the child's development. At operation, it was found that the blue nevus involved not only the skin and subcutaneous tissue, but the fascia and lower portion of the pectoral muscle. Only the skin and subcutaneous tissue were excised. The edges of the skin were united primarily without skin grafting. The histopathologic studies revealed that the tumor cells were all dermal melanoblasts. Ordinary nevus cells such as seen in the common mole or pigmented nevus were not found.



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 • silver nitrate and hematoxylin

cells, 6,250, color index, 1.03, polymorphonuclears, 62 per cent, lymphocytes, 30 per cent; mononuclears, 6 per cent. Blood Wassermann was negative.

Blood chemistry and gastric analysis were normal.

The patient was under observation until Oct. 18, 1941, when hospitalization became urgent because of severe intestinal hemorrhage and diarrhea. He was extremely pale and felt severely asthenic. Hemoglobin was 40 per cent. Immediate transfusion of 500 cc of citrated blood was performed. This was the first of many transfusions required (104 in all) during our years of observing and treating this patient.

On Nov. 19, 1941, an exploratory laparotomy was performed (J. A. L.). The liver and stomach disclosed no visible abnormalities. During the course of examination of the small intestine and colon a few small dark purplish, pinhead to matchhead sized spots were observed by transmitted light shining through the serosa. These were present throughout the entire length of the bowel. A solitary cyst of the lower pole of the left kidney was palpated and removed through a left lumbar incision. Following the operation many transfusions were necessary before he was discharged (Dec. 31, 1941).

A course of deep roentgen therapy was given with the hope of favorably influencing what we believed to be intestinal nevi similar to those seen on the abdominal skin. However, intermittent intestinal hemorrhages occurred, requiring further and more frequent blood replacement.

On Feb. 14, 1946, following sigmoidoscopy and a barium caema roentgenologic study, we believed that another exploration was advisable with the hope of finding a bleeding polyp or angioma which had possibly escaped previous detection. Immediately after this exploration the patient suffered a profuse intestinal hemorrhage, with hemoglobin dropping to 20 per cent. After repeated transfusions and proper presurgical intestinal preparation, a laparotomy was performed (March 14, 1946 J. A. L.). The entire gastrointestinal tract was again subjected to a minute and critical examination, with the same result as at the previous operation. Despite the presence of a few purplish spots in the small intestine, we conjectured that most of the pathological change was within the colon, and decided to perform a colectomy as a lifesaving measure. Due to the patient's poor physical condition we deemed it advisable to carry out the operation in multiple stages. The ileum was, therefore, completely transected about twelve inches from the ileocecal valve, and the proximal end implanted end to side into the rectosigmoid directly above the peritoneal reflexion.

Twelve days later the colon was removed up to the splenic flexure, the distal end being left in the wound as a mucous fistula when the operation had to be discontinued because of the patient's poor physical condition. A transfusion of 500 cc of blood was administered during the surgical procedure. At the conclusion of the laparotomy, a nevus was removed for histologic examination from the skin of the abdominal wall.

Following discharge from the hospital the patient remained well except for an occasional drop of blood in the stool. On Sept. 10, 1946 the remainder of the descending colon up to the anastomosis was removed. Convalescence was uneventful except for one episode of brisk intestinal bleeding which required three transfusions. He was discharged from the hospital Sept. 26, 1946. There has been no bleeding to date.

Pathology Reports.—Specimen 1, cyst of left kidney, was removed at the first operation. Macroscopic examination showed the specimen to consist of a mass of tissue measuring 5 by 4 cm., which mainly composed the wall of a cyst. The wall was thin, fibrotic, and transparent. A small amount of fat tissue was adherent to it. The intimal lining was smooth. Renal parenchyma tissue was not grossly recognizable within the specimen. At one site there was a fibrotic plaque which contained a pinhead sized cyst.

Microscopic examination showed that the wall of the cyst was lined by a zone of dense collagenous fibrous tissue. Within parts of the latter there were atrophic and dilated tubules, in the interstices of which round cell infiltration was present. Atrophic and intact glomeruli were also present. Another small cyst was observed in the wall, which was lined by regular cuboidal cells.

Diagnosis was fibrotic simple cyst of the kidney with atrophy of adjacent parenchyma.

BENIGN INTESTINAL TUMORS OF VASCULAR ORIGIN

JOSEPH A. LAZARUS, M.D., AND MORRIS S. MARKS, M.D., NEW YORK, N. Y.

HISTORICAL

ROKITANSKY (1861), in discussing vascular tumors of the intestine stated that they were of the rarest occurrence, and when found consisted of telangiectasis of the intestinal mucous membrane. The first report of angiomas of the intestine was by Gascoyen (1860). Thirty eight years later Longuet (1898) called attention to the rarity of the condition and, citing three instances questioned the authenticity of one. These three examples were discussed by Heurtault (1899) who also commented on their rarity. MacCallum (1906) reported a case from the pathologic laboratory of Johns Hopkins Hospital, and reviewed five others. Dewitz (1906), writing on benign tumors of the intestine commented on the rarity of intestinal angiomas. Following a review of the literature King (1917) found records of only three, and these he maintained were incomplete.

Helvestine (1921) grouped fourteen examples from the literature and added one which he found at necropsy. Brown (1924), after a careful review of the literature summarized nineteen case reports of the vascular tumors in question (exclusive of the stomach) and added one of his own. These included all varieties from capillary nevi to cavernous angiomas. Bancroft (1931) listed eight additional case reports and reported one of his own. To this balance sheet we add nine more, including one of our own to bring the total to thirty eight.

CASE REPORT

J. C., a white man, age 59 years, first consulted us Oct. 17, 1938, complaining of melena, belching and abdominal distention.

Family history indicated no bleeding tendency in any of its members and was otherwise completely irrelevant. The patient had been treated for gastric ulcer ten years previously.

The illness for which he consulted us began one week previously when he noticed bright red blood in stools. There was no pain on defecation or constipation, the patient having two bowel movements daily. Some abdominal distention and belching were present. There was no loss of weight, appetite was good.

Physical examination showed a chronically ill man in the late fifties, presenting marked pallor of the skin. Heart and lungs were unaffected. Blood pressure was 110/90. Abdominal examination revealed no abnormalities or tenderness except for several tenders scattered over abdominal wall. Nasal mucosa was intact and normal. Rectal examination was negative.

Sigmoidoscopy disclosed no evidence of neoplasm or other pathologic changes. Barium enema showed several diverticula in the descending colon and sigmoid. Complete gastro-intestinal roentgenologic examination showed no abnormal conditions.

Urinalysis revealed specific gravity 1.028, albumin negative, sugar negative. Microscopic 2 to 3 white blood cells per high power field. Blood count was as follows: Hemoglobin 57 per cent (83 Gm. per 100 cc.), red blood cells 2,650,000, white blood

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cells, 6200, color index, 1.03, polymorphonuclears, 62 per cent, lymphocytes, 30 per cent, mononuclears, 6 per cent. Blood Wassermann was negative.

Blood chemistry and gastric analysis were normal.

The patient was under observation until Oct. 18, 1941, when hospitalization became urgent because of severe intestinal hemorrhage and diarrhea. He was extremely pale and felt severely anemic. Hemoglobin was 40 per cent. Immediate transfusion of 500 cc. of citrated blood was performed. This was the first of many transfusions required (104 in all) during our years of observing and treating this patient.

On Nov. 19, 1941, an exploratory laparotomy was performed (J & L). The liver and stomach disclosed no visible abnormalities. During the course of examination of the small intestine and colon a few small dark purplish pinhead to matchhead sized spots were observed by transmitted light shining through the serosa. These were present throughout the entire length of the bowel. A solitary cyst of the lower pole of the left kidney was palpated and removed through a left lumbar incision. Following the operation many transfusions were necessary before he was discharged (Dec. 31, 1941).

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Twelve days later the colon was removed up to the splenic flexure, the distal end being left in the wound as a mucous fistula, when the operation had to be discontinued because of the patient's poor physical condition. A transfusion of 500 cc. of blood was administered during the surgical procedure. At the conclusion of the laparotomy, a nerve was removed for histologic examination from the skin of the abdominal wall.

Following discharge from the hospital the patient remained well except for an occasional drop of blood in the stool. On Sept. 10, 1946 the remainder of the descending colon up to the anastomosis was removed. Convalescence was uneventful except for one episode of brisk intestinal bleeding which required three transfusions. He was discharged from the hospital Sept. 26, 1946. There has been no bleeding to date.

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Microscopic examination showed that the wall of the cyst was lined by a zone of dense collagenous fibrous tissue. Within parts of the latter there were atrophic and dilated tubules, in the interstices of which round cell infiltration was present. Atrophic and intact glomeruli were also present. Another small cyst was observed in the wall, which was lined by regular cuboidal cells.

Diagnosis was fibrotic simple cyst of the kidney with atrophy of adjacent parenchyma.

Specimen 2 was removed at the third operation. Macroscopic examination revealed (1) The specimen consisted of an ileocectomy specimen consisting of 7.5 cm of ileum and the ascending and transverse colon. The mucosa showed no unusual features. Within the cecum at a distance of 15 cm from the ileocecal valve there was a pea sized polyp with a hyperemic surface which rested on top of a mucosal fold. There was no induration of the submucosa. This polyp was not hemorrhagic. Throughout the colon there were several small hyperemic bluish localized ecchymotic spots the largest of which was the size of a split pea. These were considered cavernous angiomas. They were limited to the mucosa and submucosa showed no ulceration and were situated at 17, 40, and 61 cm from the ileocecal valve. The remainder of the colonic mucosa was smooth and pale. No lymph node enlargements were present.

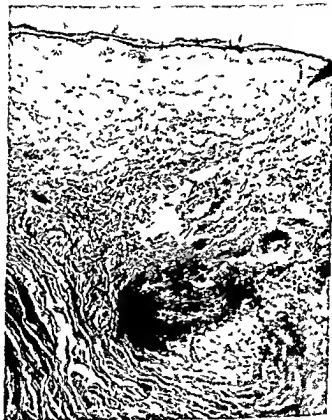


Fig 1—Microphotograph of section through skin. Epithelium is intact. Within the subcuticular stroma are several congested blood vessels with dilated lumina lined by flat endothelium with regular nuclei (X135 magnification).

Microscopic examination revealed (1) Sections through the cecum revealed that the polyp consisted of glandular mucosal tissue which was in continuity at the base with the adjacent mucosa. The glands and surface epithelium were regular and lined by columnar cells with regular nuclei. The stroma was delicate and contained numerous congested

blood vessels of capillary variety. The stroma also contained round, plasma, and some red blood cells. The base of the polyp and the subjacent submucosa contained several larger congested blood vessels, including those with smooth muscle coats. The adjacent cecal wall was free from inflammatory changes.

(2) Sections through the lesions at 17 cm., 40 cm., and 63 cm. showed that the histologic characteristics of these lesions were similar. The mucosa was intact. The stroma contained round cells, plasma cells, and some congested capillaries. Within the submucosa there were numerous congested blood vessels, some of which were dilated. They were all lined by regular flat endothelium. Some had a distinct muscular coat, others were devoid of the muscular coat. The stroma in these areas contained occasional round cells, but showed no distinct interstitial hemorrhage or blood pigment deposits. There were no inflammatory changes around these blood vessels. These lesions were definitely hemangiomatous in character (Fig. 2).



Fig. 2—Microphotograph of section through lesion at 17 cm. Mucosa is intact. Its stroma contains round and plasma cells and congested capillaries. Within the submucosa are numerous congested dilated blood vessels lined by regular flat endothelium (telangiectasia) ($\times 135$ magnification).

Specimen 3 was removed at the fourth operation. Macroscopic examination showed that this consisted of a resected portion of large intestine, comprising the splenic flexure, descending colon, and sigmoid colon. It measured 45 cm. in length by 5 cm. in width. At a distance of 24 cm. from the distal end there was a pedunculated polyp with its ulcerated and hemorrhagic tip about the size of a cherry. It consisted of brownish and grayish pink cellular tissue and was attached to the mucosa by a 2 cm. long, smooth, fibrous stalk. The mucosa contained a split perianal, smooth, bluish structure (capillary nevus or angioma) at a distance of 2 cm. from the base of the polyp (Fig. 3). There were several scattered diverticula in this portion of the gut.

Specimen 2 was removed at the third operation. Macroscopic examination revealed (1) The specimen consisted of an *Eschscholzmia* specimen consisting of 7.5 cm. of stem, and the ascending and transverse colon. The mucosa showed no unusual features. Within the cecum at a distance of 10 cm. from the ileocecal valve there was a pedunculated polyp with a hyperemic surface which rested on top of a mucosal fold. There was no indication of the submucosa. This polyp was not hemorrhagic. Throughout the colon there were several small hyperemic bluish localized erythematous spots the largest of which was the size of a pea. These were colic lateral cavernous angiomas. They were limited to the mucosa and submucosa, showed no ulceration and were situated at 17, 41 and 65 cm. from the ileocecal valve. The remainder of the mucosa was smooth and pale. No lymphatic dilatations were present.

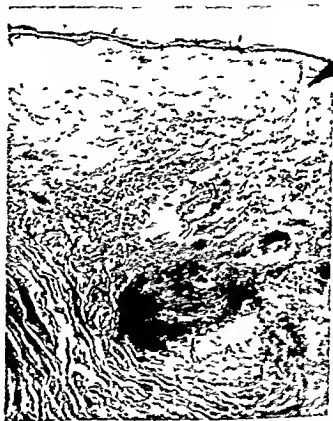


FIG. 1.—Microphotograph of section through skin. Epithelium is intact. Within the subcuticular stroma are several congested blood vessels with dilated lumina lined by fat cells. Lactum with regular nuclei (x115 magnification).

(2) A pedunculated fragment of skin tissue removed from the ascending abdominal wall contained a raised bluish superficial smooth area and possessed the characteristics of a cutaneous nevus of the skin (Fig. 1).

Microscopic examination revealed (1) Sections through the rectal polyp showed the polyp consisted of glandular mucosal tissue which was in continuity at the base with the adjacent mucosa. The glands and surface epithelium were regular and lined by columnar cells with regular nuclei. The stroma was delicate and contained numerous congested



Fig. 4

Fig. 4.—Microphotograph of section through tubular body which is composed of regular mucosal glands lined by regular mucinous columnar cells in regular array (X115 magnification).



Fig. 5

Fig. 5.—Microphotograph of section through the blue lesion. Overlying mucosa is intact. The subjacent stroma shows interstitial hemorrhage without leucocyte or round cell infiltration and contains several vascular spaces lined by a single layer of endothelium (X115 magnification).

Microscopic examination revealed the following: (1) Section through the polyp showed that it was composed of regular mucosal glands lined by mucinous columnar cells with regular nuclei. No definite ulceration was found on its surface, but a single layer of regular columnar epithelium separated the lumen from the hemorrhagic areas within the subjacent stroma. The latter showed similar hemorrhagic foci and hyperemia within the deeper portion of the stroma. Brown pigment was present within these areas, some of which represented formalin artefacts, others consisted of brown pigment within histiocytes. The stalk stroma was hyperemic and hemorrhagic (Fig. 4).



Fig. 3—Photograph showing pedunculated polyp with capillary nevus at 2 cm. from its base.

(2) Sections at random from adjacent mucosa showed the mucosa to be intact. The submucosa contained several congested venules and capillaries. There was no interstitial hemorrhage in the adjacent stroma.

(3) Sections through bluish lesions (vascular angiomata) revealed that the overlying mucosa was intact and showed no ulceration. The subjacent stroma showed prominent interstitial hemorrhages without leucocyte or round cell infiltration. It contained several prominent vascular spaces lined by a single layer of endothelium and was devoid of a muscular coat. There were also several congested blood vessels. Some were venules and con-

CHARACTER OF LESION	LOCATION OF LESION	TREATMENT	RESULT	NECROPSY
Nervus originating in submucosa and projecting into lumen of intestine	Small bowel	None	Suffocation from nervus of parotid gland	Numerous nervi found over entire body
Elevated tumor size of almond in submucosa of duodenum above papilla of Vater consisting of dilated capillary spaces, mucosa intact	Duodenum	None	Died of hemorrhage	Lesion found at autopsy
Small rounded dark spots visible when gut was laid up to light occupying about 6 ft of free margin of lower jejunum and upper ileum attached to arterial arcades situated in submucosa	Lower jejunum and upper ileum	None	Died of pneumonia	Lesion found at autopsy
Cavernous tumor presenting hemorrhage in its substance and composed of cavernous sinuses in center	Not known	None	Recovery tumor passed spontaneously from rectum	
Rapid growth on walls of rectum, with ulcerations of mucosa	Rectum	Injection with tincture of ferric iodide Paquelin cautery	Stricture of rectum died of anemia	
Speculum examination showed a nevoid growth completely surrounding rectum	Rectum		Relief but no cure	
Nevoid growth surrounded intestine like a ferrule and protruded 3 cm above surface angrona	Small intestine (submucosa and muscularis)	Resection	Died after operation	
Tumor size of a pigeon's egg in small intestine causing intussusception tumor thin walled spaces filled with coagulated blood typical nevoid tumor	Small intestine (submucosa)	Resection	Recovery	
Many enlarged veins showing globular dilatations	Upper third small intestine (submucosa)	None	Died of aortitis and mitral endocarditis	Yes
Small firm purplish nodule throughout small intestine best seen by transmitted light histologically they were vascular tumors of cavernous structure	Small intestine (submucosa invading muscularis)	None	Died arterio-sclerotic bronchopneumonia	Yes
Terrestrial phlebotomias appearing as many small brownish red masses	Entire gut (submucosa)	None	Died of tuberculous meningitis	Yes
Any varices	Jejunum (submucosa)	None	Died of pneumonia	Yes
Cavernous angioma	Small intestine (submucosa)	None	Died of pneumonia	Yes
Endoscopy a small purplish mass size of pea 2 cm from anus with ulcerated mucosa (angiomas)	Sigmoid (submucosa)	Cauterization followed by laparotomy	Died	Yes
Small angioma	Recto-sigmoid	Enterostomy—colostomy 5 stage colectomy	Cured Improved	
Cavernous angioma involving entire colon	Entire colon	Exploratory laparotomy	Not stated	
Numerous cavernous angiomas	Sigmoid			

AUTHOR	DATE	SEX	AGE	OUTSTANDING SYMPTOMS	DURATION OF SYMPTOMS
Gascogen	1870	M	44	None	
Laboulbène	1872	M	64	Repeated hemorrhage from bowel and vomiting of black blood	About 2 mo
Boyer	1877	M	62	None	
Paci	1882	F	1 long	Intestinal obstruction, passed tumor	Not stated
Barker	1883	M	43	Diarrhea and hemorrhage from bowel, mucous membrane of rectum blue and ulcerated	Since boyhood
Marsh	1888	F	10	Continuous and sometimes severe intestinal hemorrhages	8 yr
Dellbet	1890	F	21	Furcation and symptoms of intestinal obstruction	Long history of such disturbance
Nicoll	1899	F	23	Pain, vomiting, obstipation	About 2 weeks
Hektoen	1907	M	48	None	
MacCallum	1901	M	54	Digestive disturbances	Many months
Bencke	1906	M	52	None	
Ohkubo	1907	F	62	None	
Ohkubo	1907	M	79	None	
Tuffier	1913	M	37	Intestinal hemorrhage and anemia	20 yr
Hartmann	1917	F	22	Rectal hemorrhages	Not stated
Kausch	1916	M	17	Bloody stools, hemorrhage anemia	16 yr
Dujarier and Tepons Khan	1920	M	1	Rectal bleeding anemia loss of 3 yr weight	

I (CONT'D)

CHARACTER OF LESION	LOCATION OF LESION	TREATMENT	RESULT	NECROPSY
Rounded tumor filling duodenum consisting of a mesh of capillaries and a few dilated sinuses supported by highly cellular stroma	Duodenal side of pylorus	Operation—tumor enucleated	Recovered	
Hemangioma	Rectum	Transfusion and packing of rectum with kaolin	Death from hemorrhage	Not stated
Pedunculated encapsulated tumor on outer surface of jejunum (cavernous angioma)	Jejunum 25 cm. from pylorus	Not stated	Died of pneumonia	Yes
Capillary hemangioma in mesenteric and including all layers of intestinal wall except mucosa	Ileum 30 cm. from ileocecal valve	None	Died	Yes
Unspherule diffuse angioma of entire colon	Entire colon	Not stated	Death	Not stated
Diffuse angioma of rectum and sigmoid	Rectum and sigmoid	Transverse colotomy and deep x-ray treatment	Improved	
Diffuse angioma of rectum	Rectum	Opioid bed rest enema chloroform injections	Death from hemorrhage	No
Annular tumor 5 in. in length involving entire circumference of intestine showing dilated blood spaces (cavernous angioma)	Small intestine	Reaction	Death	No
Cavernous hemangioma	Entire colon	Not stated	Death	Yes
Diffuse venous hemangioma	Appendix and cecum	Cheeky steotomy and exploration	Not stated	
Annular cavernous hemangioma of colon	Colon	Operation for intestinal obstruction cecostomy	Not stated	
Cavernous hemangioma of liver multiple hemangiomas of stomach duodenum and jejunum	Stomach duodenum liver and jejunum	Blood transfusions and laparotomy	Died 4 mo. later	No
Congenital angioma	Rectum	Colostomy ligation superior hemorrhoidal vein and injection of 10 cc. of 40% solution of sodium valvate	Cure (flow up after 15 mo.)	

Diagnosis was (1) resected large intestine (2) benign hemorrhagic pedunculated adenomatous polyp of colon (3) diverticulosis of colon without inflammation and (4) hemorrhagic submucosal telangiectasis of colon (cavernous angioma)

We concluded that the severe episode of intestinal bleeding during the phase of convalescence following the first operation was due to activation of new in the small intestine

TABLE

AUTHOR	DATE	SEX	AGE	OUTSTANDING SYMPTOMS	DURATION OF SYMPTOMS
Julliani and Rankin	1922	F	--	Nausea and epigastric distress	Years
Hume	1922	M	48	Repeated rectal hemorrhages	10 yr
Helvestine	1927	F	72	None	
Blair, Markle and Karsner	1928	F	2 mo	Persistent vomiting	4 days
Hennig and Schutt	1933	M	23	Rectal hemorrhage melena	16 yr
Bensaule and Antoine	1933	F	31	Rectal hemorrhage colic, anemia cretasia	6 weeks after birth
Bensaule and Antoine	1933	M	48	Profuse hemorrhage from rectum	37 yr
Brown	1924	F	32	Pain in lower abdomen stercoraceous vomiting obstipation	Sudden onset
Reichel and Stremmler	1924	M	78	Not stated	Not stated
Rue and Swan	1929	F	47	Symptoms of gall bladder disease	Not stated
Rue and Swan	1929	F	46	Passage of small amounts of blood from rectum acute intestinal obstruction 1 mo	4 mo
McClure and Ellis	1929	F	70	Anemia tarry stools constipation, blood tumors on skin	10 yr
Ranscroft	1931	M	17	Rectal bleeding diarrhea constipation anemia	Since age of 13 mo

tained a smooth muscle liver. Others were arterioles and contained a broader wall with muscular coat. The subjacent muscular wall of intestine showed no unusual features and was devoid of interstitial hemorrhage (Fig. 5).

(4) Section through the sigmoid showed a diverticulum lined by a regular mucosa similar to adjacent mucosa. The diverticulum had a smooth muscle coat and was free of inflammatory changes.

I (CONT'D)

CHARACTER OF LESION	LOCATION OF LESION	TREATMENT	RESULT	NECROPSY
Cavernous angioma	Small intestine and sigmoid	Exploratory laparotomy	Death	Yes, a number of small subserous ecchymotic spots in small intestine; also a few in sigmoid
Hemangioma	Jejunum	Not stated	Death	Yes, a reddish blue lesion in jejunum in submucosa showing vascular spaces with endothelial lining
Hemangioma	Ileum and jejunum	Not stated	Death	Yes, 6 raised reddish lesions with bluish tint in ileum and jejunum in submucosa, Micro endothelial lined spaces filled with blood
Elevated dusky violet nodules studding surface of small and large bowel submucous and subserous	Entire intestinal tract hands and hip	Not stated	Death due to retroperitoneal perforation and hemorrhage	Yes
Cavernous angiomas	Entire colon	None	Death	Yes
Nevi (cavernous) Capillary hemangioma	Entire intestinal tract Descending colon	Not stated Mikulicz resection	Death Recovery	Yes
Small capillary angiomas of colon	Colon	Colectomy	Improvement	

Character of Tumor—The lesion was reported histologically as a nevus or nevus in character in 6 patients. There were 11 instances where the tumor was designated angioma and in 11 cavernous angioma. In 5 it was called capillary hemangioma in 2 varicosities, and in 1 the condition was noted as cavernous phlebectasis. In 4 patients including the authors', the tumors appeared as small rounded, dark spots when the involved segment of gut was held up to transmitted light. The presence of skin nevi was reported 3 times (Gascogen, McClure and Ellis, Lazarus and Marks).

Brown categorized the tumors as follows

1 Multiple tumors arranged along vascular arcades of the bowel, appearing as small red nodules situated in the submucosa attached to arteries or veins and best seen by transmitted light. Histologically these lesions were described as nevi or capillary angiomas.

2 Submucous tumors growing into the lumen of the bowel, a few of which produce ulcerations of the mucosa.

AUTHOR	DATE	SEX	AGE	OUTSTANDING SYMPTOMS	DURATION OF SYMPTOMS
Bensaude, Hillemand and Genestoux	1935	F	44	Bloody diarrhea pallor	Few months
Ackerman	1937	M	70	Not stated	Not stated
Ackerman	1937	M	64	No gastrointestinal symptoms	
Ackerman	1937	M	81	No gastrointestinal symptoms	
Raney	1939	M	†	Rectal bleeding and diarrhea entire life	Entire life
Amundsen	1938	M	65	None	
Swyer	1939	M	55	Pain lower abdomen constipation blood in stool loss of weight	3½ mo
Lazarus and Marks	1947	M	58	Profuse rectal hemorrhages	1 week

ANALYSIS OF CASE REPORTS

Age and Sex—The youngest example was that of an infant 2 months of age and the oldest 81 years. There were twenty three reports of tumor in men and fifteen in women.

Symptoms—In 9 symptoms referable to the intestinal tract were absent and in 3 others were not recorded. In the remaining 26 bleeding was a constant symptom in 18 (69.2 per cent) and of these 6 occurred in women and 12 in men. Intestinal obstruction was noted 5 times and all were in women. The duration of symptoms varied from sudden onset to 48 years. In 7 patients symptoms persisted less than 1 year and in 15 more than 1 year while the duration of symptoms was not indicated in 16.

Location of Lesion—The site of the tumor was not mentioned in 1 report. The stomach duodenum jejunum and liver were involved in 1 duodenum in 1 small intestine in 14, small intestine and sigmoid in 1 colon in 8 rectum in 5, rectum and sigmoid in 1, rectosigmoid in 1 sigmoid in 2 and entire gut in 3.

3 Submucous tumors sufficiently large to occlude the lumen of the bowel and to cause intussusception with or without intestinal obstruction

4 Diffuse tumors arising in the submucosa and completely encircling and constricting the bowel to cause intestinal obstruction

Lesions Found Only at Autopsy—In fifteen patients the tumor was discovered at necropsy and in the majority symptoms referable to the intestine were entirely lacking

Treatment—Surgery was done. Resection of the tumor was performed in four patients; colectomy in two and colostomy in two. In the latter one was followed by deep roentgen therapy and the other was injected with sodium salicylate

Local therapy was administered in five patients. Three were treated by cauterization, one with transfusions and packing and one with bed rest, morphia, and calcium chloride injections

Results—Five patients succumbed after surgery. 5 died of hemorrhage without surgical intervention. One patient (Paci) passed the tumor spontaneously and recovered. In 4 instances relief was reported—1 treated with cauterization (Marsh), 2 following colectomy (Kausch, Lazarus and Marks), and 1 following colectomy and deep roentgen therapy. Recovery of 4 patients was reported—2 following resection (Nicoll, Judd and Rankin), 1 following cauterization (Hartmann) and 1 after ligation of the hemorrhoidal vein followed by injection (Bancroft)

SUMMARY AND CONCLUSIONS

Benign tumors of vascular origin arising within the intestinal tract are rare. This report deals with 38 examples collected from the literature including one by the authors. Although symptoms were lacking in 9 of the 38 patients, profuse intestinal bleeding was the main symptom in the majority. The duration of symptoms varied from sudden onset to 48 years. The majority of tumors occurred solely in the small intestine and 8 in the colon alone. Lesions have been designated as nevi, 6; angioma, 11; cavernous angioma, 11; and capillary hemangioma, 5. The presence of associated skin nevi was reported on 3 occasions.

Tumors may occur singly or multiply. The most satisfactory results were obtained when the tumors were single and amenable to resection. The prognosis for multiple tumors is poor. The condition should be kept in mind in all instances of severe intestinal bleeding where an obvious lesion cannot be clinically ascertained.

An unusual case of severe intestinal bleeding due to multiple intestinal capillary angiomas associated with skin nevi is herewith described.

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the wound as it was not uncommon to find patients with sucking wounds of the chest who either because of inadequate dressing or derangement of adequate dressing in transit arrived at the hospital with the wounds still sucking. Adequate dressing closure was accomplished by the use of large strips of petrolatum gauze and a firmly applied gauze pad. Packing was not practiced and is strongly condemned. No sudden deaths occurred in this series during any changes of dressing. Patients who were labeled open pneumothorax and had adequate occlusive dressings were not disturbed prior to surgical closure. Physical examination of the chest was done in all cases although at times hastily. It has been the experience of this service that with proper care and the help of the ward nurse this examination may be conducted without undue strain on the patient and is of immeasurable value to the attending surgeon. Tetanus toxoid was given all patients who had not previously received it a most infrequent occurrence. Morphine was used where indicated but never in doses greater than $\frac{1}{4}$ gram. Codeine was never used. All patients were made to lie on the affected side in a semirecumbent position. Shock was combated by the use of large quantities (1000 to 3000 cc) of plasma and whole blood. It must be emphasized that in patients with serious chest wounds whole blood transfusions are imperative. Plasma per se is inadequate in stabilizing patients who have had serious blood loss. Quantities of whole blood up to 2500 cc were often administered with gratifying results. During the African and Sicilian Campaigns large quantities of fresh whole blood were made available through the maintenance of a living blood bank which consisted of twenty Corps service troops divided among the four blood types each man being replaced by a new one as soon as he had donated blood. This service was maintained twenty four hours a day every day during the bloodiest phases of the Tunisian Campaign. No patient in shock unless actively bleeding was operated upon until he was well stabilized.

All new patients were examined between operation and scheduled for surgery in the order of urgency. On several occasions a valvular tension pneumothorax was decompressed on the spot because of the patient's critical condition.

All patients with few exceptions had an anteroposterior and lateral film of the chest fluoroscopically and a flat plate of the abdomen taken on the way to the operating tent and wet film readings were done during the skin preparation phase of the operation.

The less seriously wounded patients were examined as soon after admission as possible a tentative diagnosis was made and the following routine orders instituted: (1) have patient lie on affected side or flat on back never on good side (2) check temperature pulse respiration and blood pressure every two hours (3) give no codeine or barbiturates (4) use morphine sparingly and only on order (5) encourage cough and expectoration (6) treat dehydration by intravenous glucose saline solution and plasma (7) get x-ray views of chest anteroposterior and lateral (8) watch carefully for any changes especially in respiratory rate pulse rate or development of cyanosis and report them immediately.

WAR INJURIES OF THE CHEST

A REPORT OF A SERIES OF 678 CASES

LIEUTENANT COLONEL JOHN M. SNYDER AND MAJOR FRANK TROFKA JR
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AFTER each war review of the surgical management of its multitudinous casualties has constantly yielded much to be applied in the next of the inevitable succeeding wars. Numerous reports (Sanger¹, Snyder² and Welch and Tubb³) have demonstrated the much lower mortality of thoracic wounds in the recent great war as compared to World War I of 1914 to 1918. Nevertheless it seems worth while to report the additional experience of a relatively large group of cases which were handled in a forward semimobile evacuation hospital throughout a period of eight campaigns especially as the early management largely determines the eventual outcome. Beginning in the North African Invasion and continuing throughout the Tunisian Campaign only the precepts of previous wars were available to us as a guide. By constant application of the newer chemotherapeutic advances and an appreciation relatively early that the goal of early treatment was a rapid re-establishment of normal circulatory and respiratory physiology and prompt re-expansion of the lung gratifying results were evident relatively early in our experience. Air replacement after aspiration of hemothorax was never used and greater amounts were constantly aspirated. Thus as we progressed through the Sicilian Campaign, Normandy Invasion, Northern France, Rhineland, Ardennes and Central European Campaigns therapeutic approach to these cases became more positive. The first 133 patients were treated in the Mediterranean Theater, the remainder cover the period from D Day plus 5 to the end of the war in Europe. The causes of failure in treatment as represented by fatality were constantly examined and reported and will be discussed under the different types of wounds.

PREOPERATIVE MANAGEMENT

The patients with thoracic wounds were early segregated and this allowed standardization and efficiency of management especially postoperatively. Unless obviously suffering little or no effect from their wounds, those patients with wounds of the chest were sent to the shock ward for pre-operative preparation. Here all facilities for rapid replacement of blood loss, oxygen administration, reinforcement or change of dressing or thoracostomy were immediately available. Here adequate complete examination could be performed so often impossible under the overwhelming crowding of the receiving office under the massive influx of casualties during heavy engagements.

On admission to the shock wards all patients received oxygen through a B.I.B. mask and plasma therapy was instituted. Detailed examination of the patient was then carried out with emphasis being placed on the examination of

the wound as it was not uncommon to find patients with sucking wounds of the chest who either because of inadequate dressing or derangement of adequate dressing in transit, arrived at the hospital with the wounds still sucking. Adequate dressing closure was accomplished by the use of large strips of petrolatum gauze and a firmly applied gauze pad. Packing was not practiced and is strongly condemned. No sudden deaths occurred in this series during any changes of dressing. Patients who were labeled open pneumothorax and had adequate occlusive dressings were not disturbed prior to surgical closure. Physical examination of the chest was done in all cases although at times hastily. It has been the experience of this service that with proper care and the help of the ward nurse this examination may be conducted without undue strain on the patient and is of immeasurable value to the attending surgeon. Tetanus toxoid was given all patients who had not previously received it a most infrequent occurrence. Morphine was used where indicated but never in doses greater than $\frac{1}{4}$ grain. Codeine was never used. All patients were made to lie on the affected side in a semiprone position. Shock was combated by the use of large quantities (1000 to 3000 cc) of plasma and whole blood. It must be emphasized that in patients with serious chest wounds whole blood transfusions are imperative. Plasma per se is inadequate in stabilizing patients who have had serious blood loss. Quantities of whole blood up to 2500 cc were often administered with gratifying results. During the African and Sicilian Campaigns large quantities of fresh whole blood were made available through the maintenance of a living blood bank which consisted of twenty Corps service troops divided among the four blood types each man being replaced by a new one as soon as he had donated blood. This service was maintained twenty-four hours a day every day during the bloodiest phases of the Tunisian Campaign. No patient in shock unless actively bleeding was operated upon until he was well stabilized.

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All necessary operative procedures in this group were performed in order of priority of emergency. In this group simple débridement and thoracentesis were the two most common procedures, which in themselves require little preparation.

ANESTHESIA

The importance of the proper choice of anesthesia is well recognized and in operations upon those with serious wounds of the thorax, the anesthetist and surgeon are more often confronted with poor risk patients since many are suffering from varying degrees of shock as well as an abnormal or altered respiratory exchange.

Anesthesia used in all cases in this series was either one of two forms. Endotracheal closed anesthesia with positive pressure technique, using nitrous oxide oxygen and ether was employed in all open cases including exploratory thoracotomy and the débridement and closure of open pneumothoraces. Local anesthesia and intercostal nerve block was employed for all other procedures involving only the chest wall and

administered all closed anesthesia

administration are somewhat limited if the agent of choice not available. Ernst⁴ in a discussion of the treatment of thoracic wounds based on observations made during the Polish and French Campaigns, stated that in some cases of open pneumothorax the administration of evipal sodium was useful. No intravenous anesthesia was used in our group as it was strongly felt that all forms of intravenous anesthesia are contraindicated in early war injuries of the chest.

Aspiration of the tracheobronchial tree at the completion of the operation was done on all patients who received general anesthesia.

EFFECTS OF PRIMARY THORACIC WOUNDS

Hemothorax—Hemothorax where varying quantities of blood were found in the pleural cavity as the most important abnormality occurred in 399 patients 339 of whom had penetrating wounds and 51 perforating wounds of the chest. In the cases of penetrating wounds many revealed the presence of retained foreign bodies of small size (smaller than 2 by 1 cm.) which from the standpoint of effect on early management were considered nonexistent.

These patients presented the typical signs and symptoms and x-ray findings of pleural effusion and the blood present in the pleural cavity varied from small accumulations to massive accumulations.

signs of oxygen wanting
sedimenting
from chest wall and/or lung bleeding

Hilar structures when involved usually cause death on the battlefield or if the patients arrive at a hospital installation they are in such extremis that surgery is not advisable or is futile.

Intercostal arterial hemorrhage as the etiologic factor in hemothorax the result of stab wounds of the chest is a common finding in civilian practice. Surprisingly, at no time in this series was intercostal arterial ligation for hem

orrhage necessary. In many cases during debridement or exploration the vessels were visualized and found to be torn but well thrombosed. It is believed that the tearing type of injury with rib comminution that is usually seen associated with the searing quality of many hot postexplosive missiles results in a marked contusion of the vessel wall with early thrombosis as is so often seen in extensive injuries of the extremities. In a personal communication Berry³ on active duty with the Army stated that he had not encountered intercostal arterial hemorrhage in any of the chest injuries he had treated during the Tunisian Campaign. Zeider⁴ with a Surgical Auxiliary Group also stated that he had never encountered intercostal hemorrhage in his work in the French and Belgian Campaigns.

Lung bleeding undoubtedly occurs in all cases of hemothorax but is usually self controlled and rarely recurs. However a number of patients with extensively lacerated lobes did not control themselves and lung suture was necessary to control hemorrhage.

The management of patients with hemothorax is undoubtedly one of the most important considerations of the thoracic surgeon especially in frontline hospitals. The greatest error made in the treatment of these cases is that of ultraconservatism the tendency to leave the patient alone because he is apparently doing very well. Added to this is the utter confusion on this subject that appeared especially in the earlier literature. There are several important considerations in the management of these cases.

1 The Patient. Often during the stress of battle when a hospital is filled to overflowing with battle casualties the patient as an individual is forgotten. He becomes a compound femur a belly or a chest. Patients with chest wounds are often apprehensive and a very important phase of the treatment is the reassurance that all will go well. The hemoptysis and dyspnea are explained and their importance minimized. The knowledge that they have a retained intrapulmonic foreign body often causes great concern and one must forcibly impress them with the insignificance of retained foreign bodies. Reassurance of resumption of normal lives helps to allay their fears.

2 The Wound. When patients were well stabilized and only then was attention directed to the wound. All wounds of entrance unless grossly infected or very small and clean regardless of hours after injury were excised sprinkled with sulfanilamide powder and loosely packed with petrolatum gauze. Local anesthesia was used in most debridements. There were no infections of the chest wall in this group.

3 The Hemothorax. The management of the hemothorax has been a subject of considerable controversy in the early war literature. Numerous writers some with very small series of cases advocated varied methods of treatment many of which did not take into account the basic fundamentals of respiratory physiology and the mechanics of pleural space infection. In the early treatment of hemothorax the surgeon is confronted with three basic considerations (a) progression of hemothorax (b) early reexpansion of the lung and (c) pleural space infection.

(a) Progression of the hemothorax The determination of the presence of continued hemorrhage becomes the first problem with which one has to deal. The lack of response to adequate shock therapy, or a transient response with rapid return to the shock state and increasing dyspnea are indications that active bleeding is present. When active bleeding is suspected thoracentesis is done immediately, and as much blood removed as can be aspirated. Thoracentesis is repeated in one hour and if a large quantity of blood is removed at this second aspiration, one is reasonably certain that active bleeding is present and exploration of the chest wall or lung or both is indicated. It is only when diagnostic thoracentesis is done early after injury that one might replace the blood removed with an equal quantity of air. The resulting lung compression from the pneumothorax might be of some value in controlling bleeding from lung lacerations, and obviously of no value if the bleeding is from the chest wall.

Autotransfusion was practiced on several occasions following diagnostic thoracentesis. However it is not very strongly recommended if the time of injury exceeds twelve hours as gross infection in a hemothorax may occur very early. This was evidenced in two cases in this series in which gross infection of the pleural cavity was noted following penetrating wounds seventeen and twenty four hours respectively, after injury. Thoracoabdominal wounds offer another contraindication due to the more likely contamination.

(b) Early re-expansion of the lung The active management of all patients with hemothorax is concerned primarily with directing treatment toward early re-expansion of the lung. There is one and only one method of treatment which will favor early re-expansion of the lung namely early and repeated aspiration without air replacement. Carter and DeBakey adequately sum up the advantages of early aspiration as the procedure of choice in the treatment of hemothorax as follows: (1) it relieves high intrapleural pressure (2) it removes an excellent culture medium for bacterial growth (3) it aids in early expansion of the lung—a definite advantage in limiting the area of emphysema if infection occurs (4) it decreases the incidence of massive clotting and (5) it prevents the later fixation and contraction of the thorax.

In this series thoracentesis was usually instituted twenty four hours after wounding although there was no hesitation felt about aspirating hemothoraces earlier in many cases. In the absence of recurrent shock aspiration was usually done twenty four hours after injury because it was believed that the patients were better stabilized both systemically and locally at that time. It must be emphasized that there is no danger of recurrence of bleeding (lung bleeding) as the result of early aspiration. In no case in this series did bleeding recur following aspiration twenty four hours after injury or in the cases where it was instituted earlier.

How much blood should be removed at each aspiration has been a subject of considerable discussion. During the Algerian and Tunisian campaigns (1957 cases) quantities of blood varying between 400 and 600 cc were removed at each aspiration if obtainable never more. It was observed that the patients from whom 600 cc had been removed tolerated the removal very well and that fewer aspirations were necessary for total removal of the hemothorax. In the Sicilian

Campaign (twenty six cases) between 600 and 800 cc of blood were removed at each aspiration. Again it was noted that the patients in whom 800 cc of blood were removed tolerated the procedure well and very definitely had earlier re expansion. In the French and Belgian Campaigns (470 cases) no limit was placed on the amount of blood removed at each aspiration. All patients were aspirated as dry as possible with quantities as high as 1500 cc having been removed at a single aspiration. The procedure was very well tolerated by all patients the numbers of aspiration necessary were very definitely reduced early re expansion was favored and the incidence of clotting in the hemothorax was undoubtedly reduced. No sudden deaths occurred at any time as a result of aspiration. The most common untoward effect noted in most patients was referred pain to the shoulder of the affected side which usually subsided after several hours without sedation. A very small number of patients complained of tightness in the chest which also subsided after several hours without specific treatment.

Ferguson* in a paper on Experiences in a Theater of Operations stated that in patients with a hemothorax it was found that pain and fever were increased by repeated tapplings so that it became their policy to reserve this procedure for those cases in which there was dyspnea or in which infection was suspected. This was not the experience of this Service. Although transient pain did occur in many patients is just described fever in most cases was reduced following repeated aspirations. It is strongly urged that we do not allow ourselves to be deterred from repeated aspirations especially in the early days of treatment because of transient discomfort associated with the procedure. The pain of thoracentesis is a most welcome substitute to the invalidism of unexpanded lung and fibrothorax. It is strongly believed at this time that more complete recoveries and a small incidence of unexpanded lung and fibrothorax will result if no limit is placed on the quantity of blood removed at each aspiration. Although daily aspirations were intended the large numbers of casualties necessitating emergency surgery often made it impossible to carry out this ideal practice. However it heavy casualty admission forced omission of aspiration for one day it was never missed the next. Again the maximum obtainable quantity of blood was always removed at each aspiration.

The question of air replacement may be argued for some time to come. It is mentioned here only to condemn its use in the treatment of hemothorax. It is of no value in controlling bleeding from the chest wall. In this series no patient has shown recurrence of bleeding from re expansion of the lung after aspiration. In addition air replacement has a very definite disadvantage namely the resulting pneumothorax will temporarily prevent the apex of the lung from re expanding or collapse an already expanded apex. If a pleural space infection occurs a total empyema with its resultant high morbidity and mortality rate may result.

(c) Pleural space infection. In patients with war wounds of the chest there will undoubtedly always be an incidence of pleural space infection regardless of the care and diligence expended in their management. However this incidence will be markedly reduced and in those cases in which infection

results the space will be a small one if one institutes (1) early and repeated aspiration, (2) no air replacement, (3) removal of large metallic foreign bodies with their adherent organic material and nonmetallic elements such as clothing and rib fragments (4) chemotherapy, and (5) penicillin therapy both parenterally and locally.

Supportive treatment of patients with hemothorax included the routine administration of sulfadiazine in dosages of 8 Gm the first day followed by 6 Gm daily for the next four days. Initial dose at times was given intravenously if postoperative nausea or other complications prevented its oral administration and retention. Facilities for blood level determinations were not available but daily urinalysis and biweekly blood counts were done on all patients. Oxygen was administered by a B L B mask to all patients who exhibited dyspnea with or without cyanosis. Parenteral fluids were administered when necessary, plasma being used freely to overcome protein deficiency. All patients received a full diet supplemented by vitamins C and B. Cough and expectoration were mandatory and in patients with multiple rib fractures this process was aided by the use of intercostal nerve block. Single rib fractures were usually not blocked as most of these patients were not deterred from coughing. Deep breathing exercises every hour were routine. During the French and Belgian and German Campaigns all patients received penicillin parenterally (intramuscularly) in dosage of 40 000 units initially followed by 20 000 units every four hours for seventy two hours. Following a personal communication from Bailey⁹ of Hahnemann Hospital Philadelphia with whom one of us (F T Jr) was formerly associated on the use of penicillin intrapleurally patients with hemothorax were treated by the instillation of 30 000 units of penicillin in 4 cc of normal saline solution into the pleural cavity following each aspiration. The value of this procedure must be determined by reports of investigation in rear echelons where these patients were under observation during the periods when pleural space infections are most likely to occur. Two very important questions must be answered before this procedure can be routinely used. (1) Does the irritating nature of locally instilled penicillin increase pleural exudation? (2) Does the local use of penicillin increase clotting in the hemothorax? Clinical observations in more than 100 patients in whom penicillin has been instilled intrapleurally following thoracentesis have given the impression that the incidence of clotting in the hemothorax has increased. The question of using sodium citrate intrapleurally to prevent or decrease clotting in the hemothorax was considered but not used.

There were 14 deaths in the group of 339 penetrating wounds. 11 nonoperative and 3 operative. The nonoperative deaths represent patients who were admitted to the hospital in profound shock and who died shortly after admission despite vigorous shock therapy. The operative deaths represent patients in whom at least wound excision and thoracentesis were carried out. Death in one patient occurred as a result of shock following thoracotomy for removal of a very large foreign body. It is believed that this death could have been prevented if sufficient blood could have been administered during surgery. The blood available at this time was stored blood the administration of which presented

many technical difficulties during the early days of its use so that despite numerous attempts and adaptations the patient received only 300 cc of whole blood during and immediately after the procedure. These technical difficulties were for the greater part later overcome but a large percentage of reactions still occurred. The second patient with a relatively simple infection of the pleural space that had been tapped practically dry developed an acute pulmonary edema on the fifth day after injury and died. Despite autopsy, the etiology for the pulmonary edema could not be determined. The third patient a prisoner of war doing very well developed convulsions on the eighth postoperative day during a transfusion and died within ten minutes. Cross matching had been satisfactory.

In those with perforating wounds complicated by hemothorax (fifty one cases) there was one death from shock and hemorrhage in a case with bilateral hemothorax the result of four perforating wounds. Two other patients with bilateral hemothorax however recovered.

Infected Hemothorax—In forward hospital installations where early battle casualties are treated and evacuated as soon as they are transportable the incidence of sepsis in a hemothorax is extremely low as this complication is usually not seen until the second week after injury or later. Serfat¹⁰ in a personal communication following a tour of the chest centers in the North African Communications Zone stated that many patients developed pleural space infections many weeks after injury and that the prevalent opinion at that time was that the routine use of chemotherapy delays or modifies the appearance of the complication. Seven patients in this series presented findings of infection in the hemothorax during their hospital stay. Two patients were admitted with infected hemothoraces and are of interest because of the unusually short time after injury in which both these cases presented a grossly infected hemothorax. These patients were admitted seventeen and twenty four hours respectively after injury in extreme shock markedly dyspneic and irrational. Aspiration revealed a chocolate colored fluid with a colonic odor which permeated the entire tent. The first patient died twelve hours after admission. The second patient was aspirated on two successive days followed by the establishment of closed drainage. The patient was evacuated on the sixth day after admission in fairly good condition.

Management of these cases in this type of medical installation consisted of repeated aspirations followed by closed intercostal drainage several days before the patient was evacuated. Open drainage is never done early which means never in semimobile Evacuation Hospitals.

The use of penicillin parenterally and locally will probably markedly reduce the morbidity and mortality in this group of patients.

Closed Pneumothorax—Fifteen patients in this series presented a closed pneumothorax of varying size. Facilities were not available for measuring intrapleural pressures. It was noted that in a majority of these cases wounds were in the upper anterior portion of the chest the incidence of location being divided fairly evenly between the supra and infraclavicular regions. In most cases wounds of entrance were small. Management consisted of wound excision

and bed rest. In no case was it felt necessary to decompress the pneumothorax. No patient was returned from our institution to duty, all having been evacuated to the rear. There were no deaths in this group of patients.

*Open Pneumothorax (Sucking Wounds).—*Fifty-one patients with an open pneumothorax, the result of penetrating wounds, and 49 patients with this type of defect from perforating wounds were admitted to the chest service (total 100). With the exception of the combined thoracoabdominal wounds, this group of patients probably represents the most serious of all chest injuries. Although as a rule patients with chest wounds transport well, patients with sucking wounds, unless tightly sealed by dressings or properly closed by suture, transport poorly. Early adequate management at the first aid and clearing stations determined the condition in which patients arrived at the hospital installation. One cannot emphasize too strongly the fact that the most intensive measures at resuscitation are to no avail if an open pneumothorax is not completely closed at the earliest possible time. It must be understood that by complete closure one does not refer to surgical closure. Adequate closure at these stations could be accomplished by large strips of petrolatum gauze bridged over the open wound and a large gauze pad (abdominal) secured in place over it by a tightly applied three inch adhesive plaster. At the clearing station resuscitative measures are instituted and dressings reinforced if they have become loosened in transportation. Surgical closure at these stations, contrary to policy, consisting of only through and through sutures or simple airtight closure of the skin is to be condemned. Subcutaneous emphysema in these cases may extend from the forehead to the scrotum. Properly applied occlusive dressing is definitely preferred to inadequate closure without wound excision or simple packing which is inefficient. On admission to the hospital all dressings were checked specifically and reinforced or reapplied if inadequate. In cases in which skin closure had been done, sutures were removed and occlusive dressings applied while the usual resuscitative measures were being instituted.

It was found in a number of patients with apparently simple penetrating wounds not exhibiting open pneumothorax that forceful cough while the wound was directly observed would project a column of blood (hemothorax fluid) from the wound and open pneumothorax could thus be demonstrated. This clinical test was carried out on all patients before surgery, as it is most important to determine whether a case is one of so called "masked open pneumothorax." The type of anesthesia to be used and the operative procedure indicated are directly affected by the diagnosis of the type of injury present. In patients with perforating wounds the exit wound was of course the open wound but frequently both entrance and exit wounds were found to be of the sucking type.

It was the policy of our service that no patient in shock, unless actively bleeding, was ever subjected to surgery until after recovery from shock. Following recovery from shock, anteroposterior and lateral x-ray views of the chest, fluoroscopy, and a flat plate of the abdomen were taken and patients brought to the operating room. Endotracheal closed anesthesia with positive pressure technique was used in all cases, and occlusive dressings were not removed until the anesthetist had the patient well controlled. Complete wound excision was

done in all cases and fragmented rib ends were resected. Pleural toilet was usually adequately carried out through the debrided wound by the use of rib retractors or in some cases the wound was enlarged by incision and the removal of a segment of the already fractured rib. Pleural toilet included aspiration of all blood and clots by suction removal of bone fragments from the pleural cavity and lung (a common finding) removal of foreign bodies if readily accessible, saline lavage of the pleural cavity lung suture and the instillation of 5 to 10 Gm of sulfanilamide into the pleural cavity. Muscle layer closure was done using interrupted catgut sutures sulfanilamide powder having been sprinkled over each muscle layer. The skin and subcutaneous tissue was left open in all cases. In only one case with a large defect in the chest wall close to the spine and extensive lung laceration was it impossible to effect muscle closure. In this patient the lung laceration was repaired and the affected portion of the lung sutured to the edges of the thoroughly excised open wound. Exploratory thoracotomy through a separate clean incision will be discussed under the heading of Retained Foreign Bodies and Exploratory Thoracotomies. Brock¹¹ advocated closure of an open pneumothorax and drainage of the pleural cavity with an airtight system. Closed drainage was used in this group only in those cases where extensive intrapleural damage had existed. In the others pleural accumulations were aspirated as was necessary. Surgical closure was not done if the wounds were septic occlusive dressing being used in those cases (only one case).

Postoperatively these patients received the same type of treatment as described under hemothorax as did all patients in this series. In those patients in which closed drainage was instituted drainage tubes were usually removed after forty eight hours. There were 17 deaths in this group of 130 cases 4 nonoperative and 5 operative in the penetrating type 6 operative and 2 nonoperative in the group with perforating wounds. The nonoperative (6) deaths represent patients who arrived at the hospital moribund. The 11 operative deaths occurred in cases as follows: (1) A patient with open pneumothorax and associated tracheal and esophageal laceration. The neck was debrided surgical tracheotomy performed and the esophageal laceration repaired. The neck wound was packed open. The open chest wound was closed by occlusive dressing as the patient's condition did not permit further surgery. Sudden death occurred on the fifth postoperative day when the patient was apparently making a good recovery. Cause of death was undetermined as circumstances beyond our control prevented autopsy being done. Embolic phenomenon was suspected. (2) A patient with open pneumothorax and associated transection of the cord at the level of the fifth thoracic vertebra. Death occurred on the fifth postoperative day and was attributed to the cord lesion. (3) A patient with open pneumothorax with retained foreign body of large size in the hilar region of the lung. The foreign body was removed and the superior vena cava was found to be contused with no lacerating. The patient died as the procedure was completed. Autopsy revealed that the contused portion of the superior vena cava had blown out. (4) A patient with open pneumothorax fracture compound comminuted of the left femur fracture compound comminuted of the

right os calcis and left ulna. The patient died immediately after surgery from shock. (5) A patient with open pneumothorax and penetrating wound of the brain. The patient died immediately after closure of open pneumothorax of shock. (6) A patient with perforating wound with anterior and posterior open pneumothoraces, severe wound of the left thigh (femoral artery partially severed or thrombosed). The left lower lobe of the lung was one solid hematoma, the diaphragm was split in two and the stomach was in the chest. Surgical repair was done. Death was from shock in early postoperative period. (7) A patient with open pneumothorax, extensive lung lacerations, severe head injuries with persistent unconsciousness. Death followed. (8) A patient with open pneumothorax, compound fracture of both bones of the right forearm, multiple penetrating wounds of right thigh. Death was from shock. (9) A patient with open pneumothorax with severe comminution of the left sixth, seventh and eighth ribs. Death occurred while the patient was on the operating table, cardiac injury was suspected. (10) A patient with anterior and posterior open pneumothorax (perforating wound) and tension pneumothorax after closure, from open inaccessible pulmonary wound, decompression. Death was from shock. (11) A patient with open pneumothorax. It was closed. Death was sudden and unexplainable on the fifth postoperative day.

Tension Pneumothorax—Tension pneumothorax is an infrequent complication of penetrating wounds of the thoracic emergency. The diagnosis if the condition is kept in mind, examination almost impossible, however, the intense dyspnea, bulging relatively

trachea from the midline in the suprasternal notch

in the valvular type cases a flutter valve is attached to the end of the needle, this usually being fashioned from a finger cot or condom. Hospital management usually employs closed drainage with a 1½ gauge needle or catheter. For transportation purposes a suitable apparatus is the use of a flutter valve attached to a 15 gauge needle which is passed through a rubber stopper of a saline flask and then inserted into the chest. The stopper is firmly strapped to the chest wall with adhesive tape and the patient may be moved without fear of displacing the needle. Response to this management is sudden and effective. Within a few hours, a patient who was virtually fighting for his life is breathing calmly and resting comfortably. Decompression can usually be discontinued within twenty-four to forty-eight hours except in some of the valvular types, when it must sometimes be continued for seven days.

The literature makes numerous references to the development of tension pneumothorax following the closure of open pneumothorax. This complication occurred in only one patient in this series following closure of open pneumo-

thorax Prevention of this complication is achieved by repair of the lung laceration itself

There were five patients with primary tension pneumothorax (preoperative) in this series with one death The death was in a patient who was not seen until thirty six hours after injury at which time he was moribund The patient died as a needle was thrust into his chest

Pulmonary Hematoma—Pulmonary hematomas form an interesting entity Rare after penetrating wounds they are not infrequently associated with perforating wounds or severe tangential blows to the chest Involving a portion of a lobe and sometimes an entire lobe they result from interstitial pulmonary bleeding Hemoptysis is always present in these cases They are usually not associated with a hemothorax although some of the patients develop a hemothorax twenty four to forty eight hours after injury The course of these patients is usually a very smooth one Other than wound excision thoracentesis and supportive treatment no active treatment was used When severe pulmonary hematoma may contribute greatly to the cause of death In the sixth case fatality under open pneumothorax the diaphragmatic rent and lower lobe hematoma were blast effects laterally transmitted from the perforating wound There were three other deaths (1) Pulmonary hematoma right side developed bradycardia of 40 beats per minute on fourth postoperative day temporarily improved by oxygen unexplained fatal termination three days later (2) Closed chest injury tangential perforating chest wall wound produced hematoma of upper middle and lower lobes on the right without rib fracture (3) Prisoner of war struck in left anterior chest with large searing explosive missile hematoma and death

CARDIAC WOUNDS

Cardiac wounds are rarely seen in hospital installations because most of them result in death on the battlefield Eight patients were admitted to the chest service with so called cardiac wounds Five patients presented metallic foreign bodies of small size (less than 1 cm) embedded in the myocardium four patients were admitted with lacerations of the heart two of the left ventricle one of the right auricle and one of the right ventricle The patients that presented metallic foreign bodies in the myocardium aside from showing physical signs of a small hemothorax of the left side were in excellent condition There were no signs of tamponade at any time nor were there any cardiac arrhythmias Diagnosis in all cases was made by fluoroscopic study

The management of these cases was a conservative one No attempt was made in any patient to remove the foreign body Aspiration of the hemothorax was carried out as usual In a personal communication Churchill¹² informed us that one patient was in excellent condition and no attempt had been made or would be made to remove the foreign body Bland³ encountered eight patients with retained metallic foreign bodies either in or in close apposition to the heart A favorable outcome in all patients by conservative management is reported

The patient with a laceration of the right auricle also presented a large metallic foreign body (3 by 2 inches) lying free in the right pleural cavity A right sided exploratory thoracotomy was done with closure of the cardiac laceration

tion by four silk sutures. The pericardium was closed by interrupted silk sutures except for the lower angle near its attachment to the diaphragm which was left open and communicated with the right pleural cavity. The foreign body was removed and pleural toilet carried out. It was noted that the phrenic nerve as it entered the diaphragm was lacerated with paralysis of the right diaphragm. Closed drainage was not used in this case. The patient made a good recovery and in a personal communication several months later stated that he was doing well. One of the patients with a laceration of the tip of the left ventricle was listed under combined thoracoabdominal wounds. The laceration did not extend into the chamber of the ventricle. Three interrupted silk sutures were required for closure and there had been considerable hemopericardium. The patient with the lacerated right ventricle also had a wound that did not enter the chamber of the right ventricle. Four interrupted silk sutures were required for closure.

The only death in the group occurred in a patient with a lacerated wound of the right anterior part of the chest through the left anterior part of the chest with fractures of five ribs and fracture with loss of substance of the lower end of the sternum and bilateral hemothorax. There was a laceration of the left ventricle three inches in length which did not enter the cavity of the ventricle. Exploration was carried out through the debrided wound. The lacerated ventricle was sutured with interrupted silk sutures following the use of novocain locally. Cardiac standstill occurred four times during surgery and cardiac rhythm was re-established by hand massage. Adequate closure was carried out. The patient died two hours after surgery without regaining consciousness.

COMBINED THORACOABDOMINAL WOUNDS

Sixty-five patients were admitted to the chest service with combined thoracoabdominal wounds. 31 of the left side 34 of the right side. Although the series is small it is believed that some pertinent observations have been made that may be of value in the future management of these cases. Subdivision of the wounds into those of the left side and right side is done for purposes of presenting the more common findings in the lesions and their management.

Shock of a profound nature is the rule in these patients with hemorrhage the result of liver lacerations as a contributory and often the etiologic factor on the right side and perforation of a hollow viscus and or splenic laceration on the left side. The liberal use of whole blood must be stressed in the treatment of these cases. Unless active bleeding was present surgery was deferred until recovery from shock had taken place.

Recovery is usually directly proportional to the degree of intraperitoneal involvement. In most patients wounds of entrance are in the lower portions of the chest with little resulting damage to intrathoracic structures. Open pneumothorax is probably the most common serious thoracic lesion. Injury to hollow viscera occurs infrequently on the right side.

There were two patients in this group who presented a condition which it is believed has not heretofore been described in the literature and which has been termed tension pneumothorax of peritoneal origin to denote its etiology. In both patients wounds of entrance were in the left lower part of the chest and

teriorly with large perforations of the anterior wall of the stomach with a resultant outpouring of a large volume of air into the chest through the lacerated diaphragm. The condition was recognized in one patient and closed drainage instituted however not until several hours after admission. In the other patient it was not recognized and the patient died during laparotomy. Churchill¹⁴ who was present at the autopsy performed on one of these patients when asked if he thought this condition was possible was of the opinion that tension pneumothorax of peritoneal origin was possible with the previously mentioned lesions although prior to autopsy there had been some controversy as to its feasibility. This condition is obviously not anticipated in combined wounds of the right side.

One cannot overlook the possibility of an internal sucking wound on the left side in which small quantities of air and intestinal contents are aspirated into the chest during the act of respiration. No matter how small the quantity of air may be altered intrapleural pressures result with noticeable effect on the patient. During laparotomy in left sided combined thoracoabdominal wounds an internal sucking wound becomes a true sucking wound on opening the peritoneum. It must be stressed that next to the control of active hemorrhage closure of the lacerated diaphragm should be the first duty of the surgeon on opening the abdomen. Pleural space infection from contamination by intestinal contents is to be anticipated. In lesions of the right side an internal sucking wound is prevented by the liver and its attachments.

In the management of these cases early operation after complete recovery from shock is imperative unless active bleeding is present in which case surgery must often be instituted before shock has been properly controlled. X-ray and fluoroscopic studies of the chest and abdomen were done prior to operation. Endotracheal closed anesthesia (nitrous oxide oxygen ether) was routine.

McGrath stated that penetrating wounds communicating with the peritoneal cavity require exploration of both cavities. Separate exploration of both chest and abdomen was avoided in this series whenever possible.

Throughout the greater number of the campaigns we approached most left sided lesions through an abdominal incision especially if the wound of the chest was small nonsucking and the diaphragmatic rent could be closed reasonably well from below. If considerable abdominal involvement is suspected transdiaphragmatic approach has definite limitations although for wounds involving or only traversing the left upper quadrant of the abdomen and lower chest a transpleural transdiaphragmatic approach has allowed at least six splenectomies with ease and safety as well as nephrectomies and gastric colon and upper small intestinal repair. Frequently with small open pneumothoraces these have been debrided the pleural cavity cleaned sulfanilamide powder introduced and the wound closed with the main procedure then carried out transabdominally. These patients almost all required closed intercostal drainage. If however one anticipates a large pulmonary wound transthoracic approach allows its repair and lessens the danger of a postoperative tension pneumothorax.

In right sided lesions intestinal involvement is the exception rather than the rule the abdominal damage being confined to the liver. Transpleural approach in these injuries was always done with repair of the lacerated liver and

tion by four silk sutures. The pericardium was closed by interrupted silk sutures except for the lower angle near its attachment to the diaphragm which was left open and communicated with the right pleural cavity. The foreign body was removed and pleural toilet carried out. It was noted that the phrenic nerve as it entered the diaphragm was lacerated with paralysis of the right diaphragm. Closed drainage was not used in this case. The patient made a good recovery and in a personal communication several months later stated that he was doing well. One of the patients with a laceration of the tip of the left ventricle was listed under combined thoracoabdominal wounds. The laceration did not extend into the chamber of the ventricle. Three interrupted silk sutures were required for closure and there had been considerable hemopericardium. The patient with the lacerated right ventricle also had a wound that did not enter the chamber of the right ventricle. Four interrupted silk sutures were required for closure.

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CHEST AND ABDOMEN—NOT COMBINED

The group of patients with chest and abdominal injuries not combined present the same problem in management as do those with combined thoracoabdominal wounds. Laparotomy was always necessary, and conservatism was practiced in the management of the thoracic aspect. There were 11 patients treated with four deaths. The mortalities are listed as follows: (1) Civilian 2 years of age open pneumothorax closure laparotomy closure of multiple perforations peritonitis. (2) Hemothorax conservative management laparotomy retroperitoneal hematoma debridement and fixation of compound fracture neck of left femur shock. (3) Open pneumothorax closure laparotomy closure of multiple perforations shock. (4) Hemothorax aspirated laparotomy splenectomy died twenty-two hours postoperatively of acute pulmonary edema.

BLAST INJURIES

Eight patients with clinical and x-ray findings of blast injury to the lungs were included in this series. The principal symptoms present were moderate to severe shock, hemoptysis, dyspnea, cyanosis, pain in the chest and marked restlessness to maniacal delirium. Physical findings are usually increased respiratory rate, impaired resonance to dullness on percussion usually more marked on one side, diffuse moist rales over both sides with scattered areas varying to an entire lobe in size over which breath sounds are markedly diminished and of a bronchovesicular nature. Three patients in this group developed a hemothorax despite the absence of any external signs of injury.

Treatment consisted of the use of warmth, oxygen therapy (oxygen under pressure preferable) which must in some cases be continued for days and the judicious use of fluids (blood and plasma) particularly in the early phases. The associated injuries which are usually present often determined the amount of fluids necessary. The use of human serum albumin in 100 cc doses every four hours for three or four doses was administered in three cases and gave the impression of being of some benefit. Sedation is nearly always necessary because of the cerebral symptoms, but it is given sparingly. Morphine was the drug used and never in doses greater than $\frac{1}{4}$ gr. Sulfonamides were used routinely as was penicillin when it became available. Cough and expectoration are imperative as the patients accumulate large quantities of frothy mucus in the tracheobronchial tree which favors anoxia by decreasing minute volume exchange. If surgery is necessary for associated injuries, general anesthesia should be avoided.

There were three deaths in this group: (1) Pulmonary and cerebral blast with unconsciousness and signs of meningitis; autopsy revealed numerous petechial hemorrhages through brain and lungs. (2) Pulmonary blast with compound fracture of left femur. (3) Pulmonary and cerebral blast, compound fracture of left femur, compound fracture of left ulna.

CLOSED INJURIES

Closed injuries usually result from the recoil of artillery pieces, smashed vehicles or the impact of any blunt object (large stone or other bomb debris).

diaphragm and establishment of drainage of the subphrenic space in addition to closed intercostal drainage of the pleural cavity. When laparotomy was necessary, it was done through a separate abdominal incision rather than the forward extension of the thoracic incision. Laparotomy was rarely necessary. Drainage of the subphrenic space is an important step in the management of right sided combined thoracoabdominal wounds and should be instituted in all cases. This dictum was forcibly brought to the attention of this service in a follow up report of a patient in whom subphrenic drainage had not been instituted because it was felt at the time of surgery that the hepatic damage was minimal and drainage could be accomplished only by extending the small laceration of the diaphragm by incision. The patient developed a thoracobiliary fistula with empyema and wide open drainage was instituted at the chest center.

Postoperatively, shock was treated by the liberal use of whole blood and oxygen was administered routinely for at least twenty four hours. In left sided lesions the patients were placed on a routine of (a) nothing by mouth (b) continued duodenal suction (c) fluid balance (3500 cc daily 2000 cc 5 per cent glucose in distilled water 500 cc plasma 5 per cent glucose in saline solution equal to the amount of fluid recovered by suction) (d) penicillin intramuscularly (e) sodium sulfadiazine 5 Gm initially followed by 2 Gm every eight hours intravenously, (f) vitamins C and B₁ parenterally (g) blood and urinary studies every two days. In right sided lesions unless laparotomy was performed patients were usually able to tolerate oral feeding.

There were 22 deaths in this group of 65 cases. 14 operative or postoperative and 8 nonoperative a total mortality rate of 33.8 per cent. The nonoperative deaths represent patients who arrived at the hospital in profound shock with no response to intensive therapy and who usually died within a few hours after admission. The operative deaths are listed as follows: (1) Left—laparotomy peritonitis following the resection of a segment of ileum and suturing of multiple intestinal perforations. (2) right—mechanical ileus arising from localized abscess about a perforation of the hepatic flexure of colon (perforation not recognized). (3) left—laparotomy multiple gastric and intestinal perforations operative shock and the effect of tension pneumothorax of peritoneal origin. (4) right—thoracotomy and laparotomy hemoperitoneum sudden death on the fifth day. (5) left—cord injury splenectomy nephrectomy closure of open pneumothorax shock. (6) right—laparotomy multiple intestinal perforations shock. (7) left—laparotomy ruptured left lobe of liver compound fracture of skull compound fracture of left tibia shock. (8) right—thoracotomy open pneumothorax right lobe of liver split through its entire length shock from persistent bleeding despite packing. (9) left—open pneumothorax closure laparotomy multiple gastric and intestinal perforations shock. (10) left—open pneumothorax laparotomy, intestinal resection shock. (11) left—open pneumothorax thoracotomy, splenectomy closure of gastric perforations shock. (12) left—open pneumothorax debridement and closure laparotomy suture of extensive lacerated left lobe of liver shock. (13) left—transpleural splenectomy died twenty four hours after surgery. (14) left—hemothorax debridement wound laparotomy splenectomy died twenty four hours postoperatively acute pulmonary edema.

of comminuted rib fractures mean spicules of rib in the pleural cavity or lung. Surprisingly these fragments do not visualize on x-ray examination usually because of the increased density present as a result of the hemothorax present. In one case a fragment of rib two inches long was removed from the pleural cavity. It had not visualized on x-ray examination but its presence was known because the fractured rib from which it originated presented a defect corresponding to the foreign body. The presence of clothing can only be suspected when large irregular foreign bodies are visualized. Experience has shown that large irregular foreign bodies (2 by 1 cm. or larger) often carry clothing in with them.

The size of the foreign body had a direct bearing on the decision for removal. Large irregular foreign bodies greater than 2 by 1 cm. were usually removed because they (a) often caused cough, hemoptysis and pain, (b) probably carried clothing in, (c) usually caused rib comminution with rib fragments driven into the lung or pleural cavity, (d) produced a psychosomatic effect on the patient and (e) most often caused large lung lacerations.

The location of a foreign body was of considerable importance. We felt because of the complications which might arise therefrom. Foreign bodies located near the great vessels, near the esophagus or lying free in the pleural cavity were removed early. It was during exploration for hemorrhage associated with a large retained foreign body that an active laceration of the aortic was successfully closed. Foreign bodies of small size embedded in the myocardium are usually treated conservatively, that is not removed.

The signs and symptoms present in each case are usually those produced by intrapleural derangement: cough, dyspnea, hemoptysis (frequent) and pain in the chest.

As to the optimum time for removal when one has decided that a foreign body should be removed, Carter and DeBakey¹⁴ stated that it has been considered far safer to remove a foreign body in a lung after equilibrium has been established which usually occurs in from three to ten days. It has been the belief of this service that there are two optimum times for removal of retained foreign bodies of large size (2 by 1 cm. or larger): (1) at the time of primary operation and (2) eight or more weeks later. It is understood that when one speaks of removal of foreign bodies at the time of primary operation it is presupposed that the patient's condition warrants thoracotomy. The reasons for removing foreign bodies at the time of primary operation are as follows: (1) general anesthesia must usually be employed for débridement because the wound is usually too large for excision under local anesthesia or as is often the case open pneumothorax is present; (2) because of the size of the foreign body, rib fragments (usually) and clothing are probably contaminants; (3) the foreign bodies can be removed with little manipulation without the need of incision of pulmonary tissue as the fragments are easily and readily removed through a visible wound in the lung; (4) a complete operation is performed including repair of the lacerated lung with little added risk to the patient thereby avoiding a secondary operation for late removal while preventing further major blood loss or accumulation of air in the pleural cavity; (5) sources of infection

No patient of those treated presented the so-called "stove-in chest." Multiple rib fractures were present in nine patients and single rib fractures in two. Paradoxical breathing was not marked in any patient. Intrapleural involvement was one or a combination of spontaneous pneumothorax, tension pneumothorax, and hemothorax. Two patients presented tension pneumothorax with hemothorax, one of these occurring on the opposite side from the site of injury.

Treatment consisted chiefly of measures to relieve whatever intrapleural derangement existed. Intercostal nerve block was used in multiple rib fractures to enhance cough. Elevation of the chest wall by means of traction devices was not necessary in any case.

There were thirteen patients in this group with two deaths. The two fatal cases have been discussed under pulmonary hematomas.

RETAINED FOREIGN BODIES AND EXPLORATORY THORACOTOMY

The management of retained foreign bodies is a subject of considerable discussion in the present-day literature. The type of foreign bodies, size, location, the symptoms produced, and optimum time for removal are important considerations.

The type of retained foreign bodies encountered in war injuries of the chest in the order of their frequency were (1) metallic fragments (2) rib fragments (3) clothing (4) wood (rare) (5) stones pebbles debris (most rare) (6) a combination of one or more metallic fragments plus clothing plus rib fragments a common finding. It is generally agreed that the lung and pleura tolerate most metallic foreign bodies well but that rib fragments clothing and debris are frequently responsible for infection and that the latter must be removed. X-ray and fluoroscopic studies readily reveal the presence of metallic foreign bodies but clothing most

The presence of rib fragments
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TABLE I. TABLE OF INJURIES

TYPES OF INJURIES	MORTALITY				MORTALITY	
	N CASES	PERCENTAGE	OPERATIVE	% PERCENTAGE	PERCENTAGE	OPERATIVE
Hemothorax	19	37	3	1	3	1
Infected hemothorax			1	1		
Closed pneumothorax	16	11	1	1	1	1
Open pneumothorax	130	81	5	4	10	6
(See King's wound)						
Tension pneumothorax		1	1	1	1	1
Pulmonary hematoma	2					1
Cardiac wound	5	8	1			
		<i>Left Side</i>			<i>Right Side</i>	
Combined thoracoabdominal	6	31	10	6	34	4
Chest-abdomen not combined	11	31	4	1		
Blunt injuries	8	9	3	3		
Closed injuries	13	13	1			
Total chest injuries	69					
Total mortality	96 per cent					

phications in patients with chest wounds evacuated from the forward hospitals. As the patients evacuated with chest wounds were not segregated except when complicated, the wide dissemination of these cases to different hospitals made specific case follow up rather difficult and prevented the determination of accurate incidence figures for the various complications. Until some time when the Army presents a complete over all picture these will not be known. However quite a few of the cases from our series were traced and the various complications in these the examination of numerous other case records and the composite opinions of those interviewed in all the hospitals visited handling these patients including three of the major chest centers may be summarized as follows:

1 Clotted hemothorax or fibrothorax. The incidence of this complication was increased after thoracotomy or repair of severe chest wounds such as open pneumothoraces. Unless adequate provision has been made to insure and maintain postoperative expansion of the lung by keeping the pleural cavity aspirated dry until the exudative phase is past the ensuing fibrothorax would necessitate a second late thoracotomy for decortication. This procedure was being carried out six to eight weeks postwounding even in the presence of minor degrees of infection with apparently a low morbidity and mortality. The relatively frequent incidence of fibrothorax is easily understood when one considers the increased amount of thromboplastic substance which must be poured forth from the traumatized tissues in these large chest wounds. Large clots are frequently encountered in the pleural cavity at the time of operation less than twenty four hours after wounding.

2 Thoracoabdominal Wounds. The most common complication was the severe empyema following repair of the perforated diaphragm above wounds of the liver when the latter was not drained by the subphrenic route. A thoracobiliary fistula followed. Best results were obtained if early drainage was instituted both above and below the diaphragm.

3 Empyema

(a) As noted thoracoabdominal wounds are frequently thus complicated. Soilage by biliary secretions on the right side and gastric or colonic contents on the left side make this quite understandable.

(b) Unsutured lacerations of the lung were considered in one chest center to be the commonest cause of mixed empyemas. Bronchopleural fistulas of small size were also being encountered.

(c) Empyema was more often associated with retained large foreign bodies, although under 2 cm. in diameter there seemed to be little relative difference.

(d) The composite opinion in hospitals receiving chest cases in general (not chest centers receiving mainly complicated cases by transfer for treatment) was that the over all incidence of empyema was definitely less than 5 per cent.

(e) The incidence of early abscess of the lung has been almost negligible.

(f) The late mortality of war injuries of the chest was found to be well under 1 per cent. It was the universal opinion that 80 to 85 per cent of those with chest wounds were being rehabilitated successfully for return to full duty.

are removed, thereby reducing the incidence of infection, (6) the weeks to months of worry and fretting on the part of many patients is obviated (psychosomatic effect)

If it is deemed advisable because of a patient's poor condition to defer removal of the foreign body, then it is believed that its removal should not be attempted for a period of eight weeks or longer, at which time maximum expansion has occurred infection if present is evident and a residual clotted hemothorax if present is evident at this time and thoracotomy indicated

It is believed that the removal of foreign bodies during the so-called period of re expansion and localization (from the time aspiration is instituted, usually the second day, to the time of either maximum expansion or localization of pleural space infection) is contraindicated because during this time the hemothorax is being emptied, re expansion promoted adhesions are forming and infection if occurring is being localized To do a thoracotomy at this stage is to invite total empyema The great majority of infections of the pleural space in battle casualties have manifested themselves relatively late, and thoracotomy during this period when infection is masked probably because of chemotherapy would not seem to be to the benefit of the patient

Exploratory thoracotomy was done in 102 cases in this service with the procedures shown in Table II

TABLE II

PROCEDURE	NUMBER
Removal of metallic foreign bodies	24
Lung suture and removal of rib fragments	23
Diaphragmatic repair with	42
Splenectomy	0
Liver repair	32
Repair of stomach	1
Hernia (entire stomach)	1
Repair of large bowel	1
Nephrectomy	1
Heart suture	4

Pneumonectomy or lobectomy was never done as no case presented indications for this radical procedure Partial pulmonary resection was done in one case

EVACUATION

Patients were evacuated to the rear between the fourth and fourteenth day after injury with an average of about a seven day stay in the hospital At the time of evacuation all patients were in good condition for prolonged transportation Too early evacuation of patients with chest wounds is not advisable as pleural exudation may continue for many days and unless aspirated and the pleural cavity kept as dry as possible a higher incidence of empyemas will result

LATE COMPLICATIONS

An official tour of American Army General Hospitals in England by one of us (J M S) for purposes of late follow up studies on wounds in general for the Army allowed an opportunity of learning the relative incidence of late com-

ENDOMETRIOSIS OF THE INTESTINAL TRACT

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KNOWLEDGE that ectopic endometrium may have wide although not unlimited extragenital spread and increasing ability to recognize its presence clinically have made endometriosis a condition of general medical interest.^{1, 11, 12, 14, 19, 22, 23} Among 140,716 histologic diagnoses made by the pathology department of the University of Michigan during the ten year period 1934 to 1944 endometriosis was noted in 848 patients (0.60 per cent) compared to 10 cases in 14,397 diagnoses (0.06 per cent) made in this department in the twenty year period 1895 to 1915 (Table I). These histologic values are obviously considerably lower than the actual incidence. Since the totals include both sexes and all ages the percentages are far lower than those based on series of abdominal and pelvic operations.^{1, 6, 9, 12, 16, 22} It has been estimated from comparative statistical reports^{1, 7, 21} that endometriosis exists in 10 to 22 per cent of all patients requiring gynecologic abdominal operations and in 8 to 15 per cent of all women during active menstrual life.

The intestinal tract is a highly significant extragenital location for endometriosis. In the material studied this site was involved in 35 patients (4.13 per cent): the appendix in 25 (2.95 per cent), the ileum in 1 (0.12 per cent) and the rectosigmoid in 9 (1.06 per cent) (Table II).

Occurrence in the small intestine usually is indicated by adhesions of the terminal ileum to pelvic structures with endometriosis of the loops of small bowel. The extramural invasion occasionally develops to the point of obstruction which is the usual reason for the referral of these patients to a surgical service.^{2, 3} Resection and anastomosis often effect immediate relief but verification by a frozen section and castration surgical or otherwise as previously discussed with the patient are necessary if recurrence is to be avoided. Unfortunately these patients have usually experienced many operations because of the adhesions from endometrial infiltrations and from repeated therapeutic procedures. Several instances of this nature have been encountered in this surgery department since the beginning of this study. The patients had experienced multiple operations at different hospitals but biopsies either were not done or were not conclusive.

Appendiceal endometriosis is practically always coincidental with more prominent adnexal disease although not infrequently the diagnosis of acute appendicitis is made in an instance of ruptured endometrial cyst with or without appendiceal disease. Of the 20 extramural specimens in this study however 10 were uncomplicated by other abnormal tissue. Of the intramural patients 3 had coexistent right ovarian endometriosis and 2 were without asso-

Read before the Clinical Congress of the American College of Surgeons on Dec. 29, 1946, Cleveland, Ohio.

SUMMARY

- 1 A series of 678 consecutive war injuries of the chest is presented
- 2 The type of injuries numbers and mortality rates are recorded in Table I
- 3 Preoperative management is discussed in detail
- 4 The forms and types of anesthesia used are described
- 5 Pathologic conditions following wounds of the chest include (a) hemothorax, (b) infected hemothorax, (c) closed pneumothorax (d) open pneumothorax, (e) tension pneumothorax (f) cardiac wounds and (g) pulmonary hematoma
- 6 Combined thoracoabdominal wounds were subdivided into those on the left side and those on the right side Tension pneumothorax of peritoneal origin and "internal sucking wounds" are described
- 7 Wounds involving both chest and abdomen but not combined are presented
- 8 Blast injuries are briefly described as to symptoms and treatment
- 9 Closed injuries of the chest are very briefly described
- 10 Retained foreign bodies and exploratory thoracotomy and late complications are discussed
- 11 All patients received chemotherapy The majority of patients also received penicillin parenterally and many locally

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copies and biopsies revealed only chronic colitis. A roentgenograph following a barium enema disclosed a constriction of the sigmoid of "undetermined etiology." The reader's attention is called to the roentgenographic pattern so typical of that seen in carcinoma of the sigmoid colon (Fig 1). At exploration an extensively adherent mass which was higher than sigmoidoscopic range and the inflammatory nature of which defied safe excision for biopsy, was observed binding a loop of colon to the uterus and pelvic walls. A loop colostomy was effected at this time. After additional studies of the distal segment remained



Fig 1—Photograph of barium enema roentgenograph. Note the constriction in the sigmoid colon. (From Holmes: *The Gastro Intestinal Tract. A Handbook of Roentgen Diagnosis*. The Year Book Publishers, Inc.)

inconclusive and therapeutic irradiation had been administered to the pelvis a combined abdominoperineal resection was completed six months after the colostomy was done. The long constricted and inflamed mass of bowel failed to disclose a mucosal lesion and microscopic examination revealed endometriosis of the sigmoid wall (Fig 2).

Endometriosis simulates malignancy, not infrequently coexists with malignancy and the ectopic cells themselves may undergo malignant degeneration

TABLE I OVER ALL INCIDENCE

	COMPLETE DIAGNOSES	NO OF CASES OF ENDOMETRIOSIS	PERCENTAGE INCIDENCE OF ENDOMETRIOSIS
University Hospital patients (1934 to 1944)	719.1	181	0.25
Specimens received from out side (1934 to 1944)	7876.5	667	0.97
Total 10 year period (1934 to 1944)	14076	848	0.60
Intramural and outside speci- mens (20 year period 1895 to 1915)	14,397	10	0.06

ciated endometriosis but all 5 had significant pelvic disease of some sort. Appendectomy, among other operations is a frequent experience of the patient with endometriosis without relief of symptoms. Cattell and Peacock⁴ have described the worth of considering ruptured endometrial cyst in the differential diagnosis of acute appendicitis in female patients of appropriate age.

It is reported that the recto-sigmoid is affected in 5¹² to 40 per cent¹² of patients with endometriosis with an average of 25 per cent. Thus it is estimated¹² that 2 to 4 per cent of all women (25 per cent of 8 to 15 per cent) during active menstrual life have rectosigmoidal invasion of some degree. This lesion may assume major diagnostic and therapeutic significance for occasionally malignant disease is closely simulated and radical treatment for supposed carcinoma may ensue. Experiences of others with this difficult diagnosis^{12, 13} and its undesirable sequelae^{2, 7} have been related. Of the 9 patients in this study 3 were preoperatively considered to have carcinoma and were partially or completely treated on that basis. The excised specimen (831 LAT) of the first patient upon whom the first stage of a Paul Mikulicz procedure had been done elsewhere was sent to this pathology department. The second patient (No 230782) was referred to this surgery service a loop colostomy having been performed elsewhere for supposed carcinoma of the rectum with a request from her physician for resection of the lower segment. Histologic examination of the specimen from the first patient and exploration with biopsy of the second patient revealed endometriosis in each instance and further radical treatment was obviated.

The third patient (No 381809) a 44 year-old nongravid married woman was admitted to this surgery service complaining of persistent rhythmic abdominal pain constipation and dyschezia enhanced by the menses. Appendectomy, left ovarian cystectomy and uterine suspension had been done elsewhere five years previously for the same complaints. Rectal examinations, sigmoidos-

TABLE II ENDOMETRIOSIS OF INTESTINAL TRACT

	ALL LOCATIONS	INTESTINAL TRACT			TOTAL
		APPENDIX	CECUM	RECTOSIGMOID	
Intramural	141	5	0		11
Outside	66	20	1		21
Total	848	25	1		27
Percentage	100	2.9	0.12	1.06	4.13

copies and biopsies revealed only **chronic colitis**. A roentgenograph following a barium enema disclosed a **constriction of the sigmoid** of undetermined etiology." The reader's attention is called to the roentgenographic pattern so typical of that seen in carcinoma of the sigmoid colon (Fig 1). At exploration an extensively adherent mass which was higher than sigmoidoscopic range and the inflammatory nature of which defied safe excision for biopsy was observed binding a loop of colon to the uterus and pelvic walls. A loop colostomy was effected at this time. After additional studies of the distal segment remained



FIG 1—Photograph of barium enema roentgenograph. Note the constriction in the sigmoid colon. (From Hodges: *The Gastrointestinal Tract: A Handbook of Roentgen Diagnosis*, The Year Book Publishers, Inc.)

inconclusive and therapeutic irradiation had been administered to the pelvis a combined abdominoperineal resection was completed six months after the colostomy was done. The long constricted and inflamed mass of bowel failed to disclose a mucosal lesion and microscopic examination revealed endometriosis of the sigmoid wall (Fig 2).

Endometriosis simulates malignancy, not infrequently coexists with malignancy, and the ectopic cells themselves may undergo malignant degeneration

There are accounts in the literature of carcinoma arising in endometrial tissue in the ovary and colon,^{11 12} and also of a spindle cell sarcoma¹³ originating in ectopic stromal cells in the rectum. Although in this series 2 patients appeared to have adenocarcinoma arising in ectopic endometrium, evidence excluding coexistence was not convincing.



FIG. 2.—Photomicrograph of endometrial gland in the wall of the sigmoid colon. This is one part of a section that was heavily infiltrated with endometrial tissue (X64).

SUMMARY

The increased recognition of endometriosis and its extragenital manifestations in the past ten years have characterized it as a general medical problem. What was once chiefly of interest to the pathologist and the gynecologist now engages the practical concern of the internist, urologist and general surgeon. Not the least of these clinical manifestations is the infiltration of endometrial tissue into the intestinal tract particularly when the qualities of malignant invasion are simulated in the rectosigmoid. The paucity of pathognomonic signs of endometriosis and its frequent occurrence as a coexistent lesion of lesser importance preclude a satisfactory percentage of correct preoperative diagnoses. However, we are obliged to keep this entity in mind in women in active menstrual life who present uncertain intestinal complaints. Even then histologic examination will often remain the only certain means of confirming the diagnosis and thus obviate unnecessary operative intervention.

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THE METHOD FOR DISSOLUTION OF COMMON DUCT STONES REMAINING AFTER OPERATION

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IT IS well known, as was emphasized by the late Lord Moynihan, that stones in the common bile duct may easily be overlooked during an operation. However, the frequency of this incident is not generally appreciated. Young¹ found that in post mortem examinations in patients who had been operated upon for choledocholithiasis, stones had been left behind in 16.4 per cent of the cases. Brunning,² in Popper's Clinic, found that in 367 cases in which the common duct had been opened, stones had been overlooked in 20 per cent. At the Lahey Clinic³ prior to 1926, the common duct was opened in 15 per cent of all patients operated upon for cholelithiasis, and stones were found in the duct in 8 per cent. Since 1926, the common duct was opened in 44 per cent of the cases, and stones were found in 18 per cent. One might conclude from these figures that previously stones were left behind in 10 per cent of the cases. Other statistics reveal even higher figures. Mayo⁴ reported that post mortem examinations in patients dying following operations for common duct stones revealed that stones had been left behind in one third of the cases. The causes of death were cholangitis and septicemia, but rupture of the common duct also has been reported. It appears to be a fact that stones are left behind in 16 to 25 per cent of all patients operated upon for choledocholithiasis even by the most experienced surgeons.

It is easy to understand, therefore, that an imperfect operation may account for recurrent symptoms in a considerable number of cases (50 per cent), according to recent statistics of the Kirschner Clinic.

Two factors which cause stones to be overlooked are: (1) Stones in the ampulla can be so deeply embedded in crypts or ulcerations that they are actually inaccessible through the routine supraduodenal incision. Even a large sound may slide past such a stone and pass easily through the papilla. When indurated pancreatic tissue surrounds the ampulla even careful palpation around a sound introduced through the papilla is not conclusive. (2) During attacks of biliary colic and vomiting stones may be forced upward into the intrahepatic ducts. Later they may descend into the common duct.

Retroduodenal or transduodenal exposure of the papilla are operations which decrease the probability of missing common duct stones. But such operations have a relatively high mortality (up to 20 per cent) and most surgeons are reluctant to use them in poor risk patients. The difficulty of dealing with stones in the ampulla is emphasized by the fact that some surgeons (Finsterer and others) have even recommended leaving stones which are difficult to remove and performing a short circuiting operation (choledochoduodenostomy). Such a procedure, however, has not been widely accepted.

Two techniques have been developed to improve the results in operations for choledocholithiasis. Mirizzi's method of cholangiography during the operation, and Pribram's method³ for the postoperative dissolution of gallstones remaining in the common duct under cholangiographic control. Cholangiography during the operation enables one to discover stones in the common duct which otherwise might be missed but even with this method it is difficult to be certain that all stones have been removed. In a case in which multiple stones have been removed even though cholangiography has been carried out during the operation the surgeon should never omit drainage of the common bile duct which provides opportunity for further cholangiographic studies in the postoperative period.

The scaffolding of the usual gallstone is made up of cholesterol, which is soluble in ether. By dissolving the scaffolding ether disrupts the structure of a stone causing it to crumble into a mud the particles of which can easily pass through the papilla. The ether method therefore is effective only against stones containing cholesterol.

Practically all stones containing large amounts of cholesterol are formed in the gall bladder. Such stones may pass into the common duct either through the cystic duct or by way of an internal biliary fistula.

The usual attack of gallstone colic indicates that a stone in the gall bladder has moved from the insensitive fundus to the opening of the cystic ducts, the most sensitive area in the whole biliary duct system. A stone in the opening of the cystic duct causes the muscular wall in the collum cystic area to contract in a painful spasm. During such an attack the stone may pass through the cystic duct into the common duct or may slip back into the fundus. In either case the biliary colic is relieved. On the other hand a stone may pass through the papilla without causing pain. The papilla is much less sensitive than the collum cystic area. These statements are based on the results of experiments which were carried out over a period of many years.

The cystic duct is the usual pathway for stones which move from the gall bladder into the common duct. In some instances a large stone may pass directly into the common duct through an internal biliary fistula between the gall bladder and the duct. It is well known that in other instances gallstones may pass directly into the duodenum or colon.

Stones may form within the common duct in the presence of stasis of bile and cholangitis secondary to obstruction at the papilla. In most instances such stones are pigment calculi containing relatively small amounts of cholesterol. A stone originating in the gall bladder may lodge at the terminal portion of the bile duct and cause stasis of bile. Pigment concretions then may form in the stagnant bile above the obstruction and such stones may extend high up into the intrahepatic ducts. Foreign bodies such as a rubber tube favor such precipitations. Incrustation of rubber tubes lying within a bile duct occurs regularly.

Among the yellow races on the other hand conditions of stone formation are quite different. Among Chinese and Japanese gall bladder stones are extremely rare whereas the great majority of stones are pigment stones and are

formed within the bile ducts. Such a "Chinese stone" which was formed primarily within the common duct has been analyzed by Dr. Wong (Digby) with the findings as listed in Table I.

TABLE I

	PER CENT
Bilirubin and biliverdin	93.12
Cholesterol	1.64
Calcium	1.20
Phosphate	2.10

In orientals, therefore, stones may form in the bile duct while the gall bladder remains normal. In patients with obstructive jaundice caused by stones in the ampulla, the unaffected gall bladder is commonly greatly enlarged. Courvoisier's law, therefore, is useless in the Far East.

The process of crumbling down of the stones through dissolution of the cholesterol scaffolding necessarily takes some time especially because only small amounts of ether can be used at the same time. This can be shown experimentally by putting some cholesterol-containing stones in a test tube and mixing them with ether. The process of dissolution of cholesterol out of the stones can be demonstrated by the appearance of the white cholesterol needles crystallizing on the wall of the test tube when the ether evaporates (Fig. 1). This can be observed very soon. However, it might take hours before the stones are transformed into a brown mud of pigment. Enlightening experiments concerning the dissolution of gallstones in the gall bladders of dogs by means of ether injections have been carried out by A. B. Raffin. Only in rare cases may we expect success within a few days.

It is of considerable practical importance to know that there is a very good method of dealing with remaining common duct stones in the postoperative period under cholangiographic control. The results of Pribram's ether method have meanwhile been confirmed by many observers.^{7,12} With that knowledge one is not compelled to force the issue of freeing the papilla on the operating table. In my own statistics this has caused the mortality rate in poor risk cases to drop to 3 per cent. In surveying fifty-one cases in which the ether method was used for the postoperative dissolution of gallstones remaining in the bile duct I have found no failures and I have not found it necessary to perform a secondary operation.* Since other surgeons who have used the ether method have had only partial success or no success at all there must be a difference in technique to account for the variance in the results.

The first consideration is that of the solvent. Ether is used for this purpose. Although chloroform and acetone are better chemical solvents for cholesterol, they should not be used. Acetone is badly tolerated by the patient and I have seen ulcerations in the duodenum with serious hemorrhage following the use of chloroform. One such patient nearly died. Ether on the other hand has been used clinically with satisfactory results. In experiments on dogs

*One patient was operated upon by another surgeon for recurrent attacks three years later but I have been unable to obtain the operation report.

Raffle found that ether produced no evidence in any of the animals of inflammatory reaction about the bladder ducts or liver sufficiently severe to make a permanent change in the tissue.

In some instances it is advantageous to mix a small amount of alcohol with the ether. This raises the boiling point of the fluid so that it exerts less pressure when it is injected. But the solubility of cholesterol in an ether alcohol mixture is less than in ether alone so the mixture should not contain more than 10 to 20 per cent of alcohol.

The opinion has been expressed that the success of the ether method is not due to dissolution of the stone but that the boiling ether blasts the way open through the papilla. This is certainly wrong. However this idea apparently has induced some surgeons to use force while injecting as much as 5 cc of ether—certainly not to the liking of the patient and probably without success since such forced injections are regularly followed by a violent spasm of the sphincter muscle.



FIG. 1.—Experimental dissolution of gall stones in vitro.

Flushing the common duct with saline solution in an attempt to open the papilla by means of hydrostatic pressure was carried out unsuccessfully by H. Kehr more than fifty years ago. The patients resented the pressure and the papilla did not open.

Increased pressure within the common bile duct causes the patient to experience a very unpleasant sensation. Moreover if mechanical pressure were effective one would expect a sudden and dramatic effect but such results do not occur.

In some of my cases the process of dissolution of stones could be followed in a series of cholangiograms showing the gradual diminishing size of the obstructing stones, the increasing patency of the papilla and the passing of larger amounts of lipiodol into the duodenum. A ray control is an important part of the postoperative treatment.

The use of the T tube for drainage of the common bile duct merits discussion. The T tube is *not* suitable for use with the ether technique for dissolution of stones. When ether is injected through such a tube much of it evaporates upward into the liver instead of reaching the stones. Ether penetrating into the intrahepatic ducts produces an unpleasant sensation of pressure and nausea and may even produce vomiting.

Also, use of the T tube deprives us of a very important sign in cholangiography. The intrahepatic ducts should *not fill at all* when the papilla is patent. When injecting lipiodol slowly through a tube which points only downward the opaque liquid should pass directly into the duodenum. Filling of the intrahepatic ducts provided correct technique is used is always a sign of a certain back pressure suggesting *incomplete patency of the papilla* (stone or spasm). I believe that the use of the T tube is one of the main factors in the failure of the ether method and also in the failure to secure satisfactory cholangiograms.

Moreover removal of the T tube may in some cases cause a tearing of the wall of the duct. It is well known that injury inflicted on a fresh scar may stimulate excessive growth of fibrous tissue. This may well account for an excessive cicatrization of the wound in the wall of the common duct and the later tendency to shrink. In recent times an increasing number of benign strictures as *postoperative sequelæ* have been reported. It must be admitted that many of these strictures probably are due to direct injury of the duct during operation. However it is difficult to believe that injuries should take place on such an amazing scale. It is possible that some of the strictures result from excessive cicatrization following injury to the duct caused by removal of a T tube.

For these reasons I believe that in common duct surgery the T tube should not be used. A simple tube or catheter is preferable and a catheter with a double lumen has some advantages. Even when such a drain is stitched water tight into the duct with silk sutures it can be removed after ten to twelve days without the slightest difficulties. It may also be reintroduced after it has been withdrawn.

Confidence in the effectiveness of the ether method for postoperative dissolution of remaining common duct stones should not deter the surgeon from carefully removing all accessible stones at the time of operation. It does, however, eliminate the necessity of *forcing* the papilla. There is no harm in trying to pass the papilla with sounds or bougies of increasing caliber as long as the procedure is carried out with the greatest gentleness. But forcible dilatation is a risky procedure because of the danger of making a false passage. This takes place much more often than is generally realized and penetration into the surrounding pancreatic tissue is especially frequent. I have interested some pathologists in this question and they have paid especial attention to the possibility of a false passage in patients who have come to necropsy after common duct surgery. They have found that it is a frequent incident and that in many instances the operating surgeon has been unaware of the accident.

The Lahey Clinic (R Adams¹⁴) has reported three cases showing fatal ascending infection with gas bacilli following forcible dilatation of the papilla.

Furthermore forcible dilatation may cause a crack or tearing of the papilla which might later cause stricture through scarring.

In badly infected patients with prolonged jaundice and danger of cholemic bleeding all forcible attempts should be avoided. Not only is forcible dilatation of the papilla dangerous but it is pointless. The passage of a sound through the papilla into the duodenum gives no assurance that all stones have been removed. Postoperative cholangiograms have given ample evidence of that.

In all cases of prolonged obstructive jaundice there is more or less liver damage. The hepatic injury is even more serious in the presence of cholangitis. Therefore the use of general anesthesia and the barbiturates should be avoided or restricted as much as possible. A patient with severe liver damage might pass from the state of anesthesia into hepatic coma. Spinal anesthesia with the addition of gas oxygen when necessary has proved to be the least harmful method in such cases and can be recommended.

For twenty years we have favored the use of the subcostal incision.¹⁵ Wide exposure, immediate access to the operative field, the ease with which neighboring structures (duodenum and right colonic flexure) can be excluded from the field and the nonexistence of postoperative hernia even in badly infected wounds are definite advantages which have been confirmed by all surgeons who have used the incision.

After clear exposure of the structures by sharp dissection of adhesions, if necessary the gall bladder is emptied by aspiration and the cystic duct is carefully dissected and divided between two silk ligatures. *No clamps are ever used on the cystic duct.* The gall bladder is opened and electrocoagulated. The liver bed of the gall bladder should be completely dry.

The common duct then is opened about halfway between the normal emptying place of the cystic duct and the duodenum. The opening should not be too near the duodenum for two reasons. First a small amount of leakage in the supra-ampullary region might disturb the clearness of the postoperative cholangiogram and second it is easier to maintain the choledochostomy tube in position when some distal stump of the common duct is present. Exploration of the common duct through a split cystic duct is not to be recommended. The cystic duct often runs parallel to the common duct for a considerable distance and may empty rather low, so that the upper portion of the choledochus is difficult to explore. It is good practice to empty the common duct by aspiration before it is opened. This makes stones more easily visible and they are less likely to slip upward into the hepatic ducts during manipulation.

With the duct opened all accessible stones are removed. A scoop or sound is passed downward to the papilla and the ampulla is carefully palpated around the sound. Many stones can be discovered in this way. However in the presence of a swollen and indurated pancreas head the success of detecting stones by palpation is limited. One may mistake indurated lobules for stones and try vainly to extricate them with a scoop.

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seems necessary. The common duet tube is fixed by means of a safety pin and is plastered firmly to the skin.

On the fifth day after operation if recovery has been uneventful the first cholangiogram is made. The patient lies in the supine position slightly on the right side. All plasters are removed and the tube is held firmly in position by an assistant. Fifteen to twenty cubic centimeters of warm lipiodol are injected slowly and two to four pictures are taken at intervals of five to ten minutes. The oily solution is preferred since aqueous solutions give precipitations when mixed with bile.

Correct interpretation of cholangiograms requires some experience. In case the ampulla is free of stones and the papilla is open the opaque liquid passes directly into the duodenum and the intrahepatic ducts do not fill at all provided the injection is carried out slowly. Any filling of the intrahepatic ducts suggests some *back pressure* which might of course be due to spasm. Actual conditions are revealed clearly in a series of pictures. In case there is still some suspicion of a sphincter spasm it can be released by intravenous injection of $\frac{1}{2}$ to 1 mg atropine sulfate or by inhalation of amyl nitrite.¹²

When there is evidence of stones the ether treatment is initiated. The treatment is best carried out in the morning with the patient fasting in order to diminish bile secretion. The bile duct is emptied by aspiration of bile through the tube. Ether is then injected drop by drop and the patient is asked to signify the point at which he feels pressure. Then ether is reaspirated and the procedure is repeated several times within the limits of tolerable pressure as indicated by the patient. It has proved helpful to use a *double barreled catheter* (see Fig. 2) one tube providing decompression by allowing immediate evaporation of ether during injection. Undue discomfort resulting from pressure can thus be almost entirely avoided. The finish is terminated by injecting 5 to 10 cc of warm paraffin or olive oil and the tube is then closed for several hours. The patient may reopen it when he feels increasing pressure.

The whole procedure can be repeated several times a day and is continued for at least a week. After that time another cholangiogram is made.

The gradual crumbling of the stones, the diminution of introductal pressure and the opening of the papilla permit injected saline solution to pass into the duodenum so that the amount returning through the drainage tube diminishes until the return drainage ceases completely. Eventually the tube can be passed easily through the open papilla into the duodenum. It is interesting to note that in no instance did the patient feel any pain or even the slightest awareness of an unpleasant sensation during this procedure. This fact can be taken as further proof for the thesis which I have always maintained that *the common attack of colic is caused by a stone passing through the cystic duct or touching the column cysticus area and not as a result of a stone passing through the papilla*.

The time required for the dissolution of stones varies greatly and depends upon several factors. It depends upon the degree of access of ether to the stones. Patients with an enlarged common duct feel the pressure much less than patients with a small duct. Greater amounts of ether can therefore, be applied in patients with dilated ducts.

One is pleased when the sound passes easily through the papilla into the duodenum. However we need not feel uneasy when this does not occur. We may terminate the operation at that point with safety. Immovable stones in the ampulla are certainly a challenge and it injures the pride of the surgeon to fail in his attempt to remove all stones and secure free passage through the papilla at the time of operation. But admitting that we are not successful in all cases it is a relief to know that there is a method of dealing with these stones safely in the postoperative period.

A double barreled catheter with two side holes is then introduced downward into the common duct until the tip touches the stones in the ampulla. The size of the tube is determined by the diameter of the common duct a catheter being selected which will allow free passage of bile from the liver.

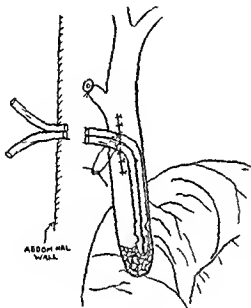


Fig. 2—The double barreled catheter in place in the common bile duct

The wall of the common duct is then closed around the catheter with five silk sutures several of them being tied around the tube in order to fix it in position. Traction on the catheter should not displace it. Watertight closure of the common duct must be attained and this should be tested by the injection of saline solution. Leakage might interfere with the clearness of the cholangiogram and it also hinders the proper placing of ether upon the stones. The suture line is reinforced by a layer of the hepatoduodenal ligament or by a serosal flap from the area of the cystic duct.

If the liver is enlarged the tube is brought out through a small stab wound in the most suitable position. For safety, another rubber tube may be inserted beside the choledochostomy tube and left in place for forty-eight hours if it

a high calcium pigment content. The accessible surface of the stones is also important. Calculi hidden in crypts or in ulcerations in the ampulla are less accessible than a mass of small stones filling the ampulla.

In many instances I have used novocain atropine amyl nitrite and other drugs in an attempt to relax a presumed spasm of the sphincter muscle. No harm is done in trying them but I have seen no convincing evidence that they shorten the time required for the elimination of stones.



Fig. 37. (For legend see opposite page.)

Abundant drainage of bile from the liver dilutes the ether and may interfere with the access of ether to the stones. Fasting and restriction of fluid intake, therefore, are helpful.

The more frequently the injection is carried out, presumably, the shorter will be the time for successful dissolution of the stones. The time required for crumbling the stones depends also on the chemical character of the calculi. Stones with a high cholesterol content are easier to fragment than those with



Fig. 2A

Fig. 3 A, B, and C.—Cholangiograms showing the successful dissolution of common duct stones by the ether method.

the ether method was finally successful. In one patient 70 years of age the papilla was still obstructed after five weeks of treatment. Blood oozing from the tube suggested a malignant growth and secondary operation was contemplated. A cold which the patient developed necessitated postponement of the scheduled operation for one week during which time the ether treatment was continued. A final cholangiogram on the day before the operation was to have been performed revealed that the papilla was completely free of stones. Three years later the patient was reported perfectly well.

I have had to treat several patients with external biliary fistulas in whom common duct stones had been overlooked at operation. The general condition of such patients is sometimes poor. The appetite and digestion are disturbed and the patients are dehydrated because of loss of fluid through the fistula. The patient's condition sometimes deteriorates very rapidly but a surgeon cannot lightly advise a second operation early in the postoperative course and maintain the hope that the stone will eventually pass spontaneously. There can be no doubt that the risk of the second operation is considerable. In such cases the ether method offers the possibility of safe treatment and in the cases in which I have used it I have had no failures.

Cholangiography is first performed to confirm the presence of stones as the cause of the obstruction and the ether method is then used. It has always been easy to introduce a rubber drain into the fistula and the catheter finds its way into the common duct. In one case in which the external biliary fistula had persisted for three and one half months the ampulla was emptied after treatment over a period of one week and the fistula closed two days after removal of the drain.

The accompanying cholangiograms (Fig 3 A to C) of recent date demonstrate the results of the ether method of dissolution of remaining common duct stones in a 54-year-old woman with an obstructive jaundice of three months duration. For three weeks there was no success and the skeptical attending physician urged a second operation. Only on the twenty-fifth day did the cholangiogram show disappearance of the obstructing stones and a complete patency of the papilla. The final cholangiogram shows how easily the catheter could be passed through the papilla.

These cholangiograms are perhaps dramatic but the method is not. It is a slow conservative method which requires patience and time. Its greatest advantage is that it is entirely safe and harmless.

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In many instances patients have been dismissed from the hospital after fourteen days with the choledochostomy tubes in place and have been treated as outpatients. Safe fixation of the tube to the skin is important but if the tube comes out it can easily be replaced provided it is done immediately. A patient who was a physician carried out the treatment himself at his home and returned only for the final cholangiogram and to be congratulated for his success.

The time required for the dissolution of calculi varies from one to six weeks. In two patients I was on the verge of undertaking a secondary operation before



Fig 3C (For legend see page 81)

BRACKETT OPERATION FOR UNUNITED FRACTURE OF THE NECK OF THE FEMUR

JOHN C IVINS M D * AND RALPH K GHORMLEY M D † ROCHESTER MINN

THE procedure of efficient closed reduction in fresh fractures of the neck of the femur, such as the Whitman or Leadbetter methods with the application of properly placed internal fixation developed during recent years has increased the percentage of fractures in which union occurs to 72.9 per cent according to statistics of the Fracture Committee of the American Academy of Orthopaedic Surgeons. This is the percentage of union obtained only by internal fixation. A study of all methods of treatment of fractured hips in the country as a whole would surely show a much higher percentage of nonunion.¹ The numerous methods of treatment and the varying results reported in current literature attest the fact that though results are better than those previous to the period of internal fixation the problem is as yet not completely solved.

Selection of proper treatment in those many cases in which nonunion persists after treatment is a problem. This is rendered somewhat more difficult by the paucity of reports in the literature dealing with the end results of significantly large series of cases in which repair procedures have been used. In a previous paper Rowe and Ghormley² reported data on the Brackett operations at the Mayo Clinic through 1942 and described briefly the three general classes of procedures for correction of nonunion of the neck of the femur. They gave especial attention to indications and limits of application of these procedures. It was pointed out at that time that the use of one of the reconstructive procedures was favored over osteotomy whenever the condition of the patient warranted it because better mechanical function was attained. That opinion is still held and the present report is being made to summarize data concerning and to evaluate the results of all the Brackett operations at the Mayo Clinic through 1945. It includes additional follow up information and re-evaluation of results in those cases reported by Dickel and Ghormley³ in 1941 and in the series reported by Rowe and Ghormley in 1944.

In twenty six years from 1920 to 1945 inclusive the Brackett (or modified Brackett) operation was performed in seventy one cases (Table I). More than 50 per cent of these operations were performed in the last three years. Twenty three (32 per cent) of these seventy one patients had undergone at least one operation elsewhere and two of these twenty three had undergone two operations elsewhere.

Of the seventy one patients forty five were women and twenty six were men. The average age at the time of operation was 53.7 years. The range

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an angle estimated to be the original angle of the neck of the femur, that is, the line of incision through the trochanter sloped downward and outward. "This incision, at the upper end, was started exactly at the base of the neck of the femur, leaving intact whatever portion of the neck remained attached to the shaft, the upper end of the shaft, with the remainder of the end of the neck, was then brought up into the incision and rounded off in the same curve which had been produced in hollowing out the head." After this newly modeled neck was levered into position in the head, the trochanter with its attached muscles was pulled downward to come into a position below and lateral to its normal position and the sharp, wedge shaped lower end protruded beyond the shaft on the lower lateral border of the place from which it was removed. It was fixed in this new position by sutures passed through drill holes.

Thus the Brackett operation as modified practically re-establishes the normal relations of the hip so that the muscular attachments are all in place and have a constant tendency to hold the upper end of the shaft firmly into the head. The operative technique employed in our cases resembled closely the Magnuson modification but the method of internal fixation has varied among surgeons. It is significant that of the thirty eight cases in which the operation was performed during 1943, 1944 and 1945 internal fixation, usually with one or more vitallium screws was used in all but three cases. In the entire series internal fixation of some sort was used in fifty five cases or 77.5 per cent (Table II).

TABLE II INTERNAL FIXATION AT TIME OF BRACKETT OPERATION

MEANS	CASES	PER CENT
Vitallium screws	44	80.0
Beef bone screws	4	7.3
Wire nail	3	5.5
Steel nail	2	3.6
Johannsen nail	1	1.8
Knowles pin	1	1.8
Total	55	100.0
SITE		
Head and shaft only	43	78.2
Trochanter, shaft and head	7	12.7
Trochanter and shaft	5	9.1
Total	55	100.0

RESULTS

One hospital death occurred in this series of seventy one cases, the mortality rate therefore was 1.4 per cent. Death was attributed to staphylococcal bacteremia secondary to infection of the wound and the patient died six weeks after the operation which was performed in 1938. Postoperative complications encountered in the series are summarized in Table III.

Postoperative hospitalization in these cases averaged eighty nine days, the shortest being forty eight days and the longest 252 days. In twenty six cases in which definite information was available the average time after operation when crutches could be discarded entirely was 33.3 weeks with a range of from six weeks to seventy five weeks.

TABLE I BRACKETT OPERATIONS BY YEARS*

YEAR	OPERATIONS
1920	2
1923	2
1926	1
1928	1
1930	1
1934	1
1936	1
1937	1
1938	4
1939	5
1940	1
1941	2
1942	5
1943	9
1944	16
1945	11
Total	71

*Includes modified Brackett operation

was from 7 to 77 years. The average duration of the nonunion at the time of operation was 182 months with a range of from three months to ninety six months.

TECHNIQUE

Brackett's¹ original technique was described in part as follows:

The tensor fasciae femoris and gluteus medius are separated, the muscle attachments on the outside of the trochanter are removed subperiosteally or with a thin bone attachment and the top of the trochanter removed so as to save the attachment of the gluteus minimus and piriformis. These muscles are then all turned backwards and upwards and the upper and anterior portion of the capsule exposed to the edge of the acetabulum. The capsule is opened longitudinally to its fibers on the upper portion of its anterior surface saving the attachment of the ligament if possible but which however cannot always be done.

The capsule above the opening is then detached from the femur and retracted outward and backward, the trochanter cut off just below the level of the upper edge of the head, the inner portion rounded to correspond to the curve of a 12 $\frac{1}{2}$ inches to 9 inches radius saving the anterior and inner cortex. The outer portion is either cut off obliquely or a wedge taken out near the outer surface allowing the outer cortex to be pushed inward. The free surface of the head is thoroughly freshened covering this area so as to make a corresponding curve to the rounded top of the trochanter. In abduction of the leg the convex surface which has been fashioned on the trochanter is brought directly into the concave head and in this position is firmly held against it. In this way the

the freshened cancellous surface of the proximal end of the femur and the trochanter for the new union.

not allow the first position to be maintained. The new union is held in place by the freshened cancellous surface of the proximal end of the femur and the trochanter for the new union. This gives to it a somewhat oblique angle partly resembling a normal leg without the normal neck. [Then after closure of the capsule] the attachments of the gluteus medius and minimus and piriformis are either secured to the upper surface of the trochanter or are inserted into the wedge shaped depression which has been made in order to round off its upper and outer end.

Magnuson,² in 1932 described a modification in which after preparation of the head of the femur, the trochanter and attached muscles were cut off at

Review of the eleven cases in which treatment failed shows that in four cases slipping of the fragments, always of the head from the shaft, occurred after good position had been obtained at operation. In three cases typical aseptic necrosis of the head occurred and in two of them it was noted at operation that the head did not bleed very well. In another case, that of a woman 71 years old, roentgenograms made two years after surgical treatment showed nonunion. The head of the femur was markedly absorbed and the remainder devitalized. No further reconstruction was advised. One patient, aged 75 years at operation, did not stop using crutches before death from other causes occurred eighteen months after operation. In one case the checkup eighteen months after operation showed no union and at reoperation, when a Whitman reconstruction was performed, some bony union between the head of the femur

TABLE VI. RESULTS IN REPAIR OF UNUNITED FRACTURES OF THE HIP

AUTHOR	OPERATION	CASES	REPORTED RESULT		PER CENT FAVORABLE
			RESULT	CASES	
Colonna 1939 ⁶	Colonna	10	Excellent Fair Poor Failure	24 (60.0%) 9 (22.5%) 2 (5.0%) 5 (12.5%)	82.5
Henderson 1940 ⁷	Intra articular osteosynthesis	67	Union Failure Death	46 19 2	68.6
Galle and Lewis 1940 ⁸	Smith Petersen nail and graft	15	Union Failure Too early	6 1 8	Not evaluated
Magnuson 1940 ⁹	Modified Brackett	41	Good Poor Death Other	28 6 2 5	68.3
Reich 1941 ¹⁰	High oblique osteotomy	26	Good Failure Death	22 3 1	84.6
Campbell and Smith, 1941 ¹¹	Trochanteric osteotomy	28	Good Fair Poor	14 (50.0%) 8 (29.0%) 6 (21.0%)	78.6
Henderson 1941 ¹²	Extra articular osteosynthesis	14	Excellent Good (union) Fair Failure Too early	8 2 1 2 1	78.6
Herrmann 1942 ¹³	Colonna	12	Good	8	66.7
	Magnuson	7	Good	4	57.1
	Bone graft	3	Good	3	100.0
	Hubbs fusion	3	Good	2	66.7
	McMurray	8	Good	5	62.5
Speed and McGehee, 1944 ¹⁴	Subtrochanteric osteotomy	18			
Leadbetter 1944 ¹⁵	Cervical axial osteotomy	8			
Stewart 1945 ¹⁶	Subtrochanteric osteotomy	11	Fair Poor Failure	3 2 2	63.6

TABLE III POSTOPERATIVE COMPLICATIONS

	CASES	PER CENT
	3	4.2
	17	23.9
	2	2.8
	1	1.4
	1	1.4
	1	1.4

In evaluation of the end results in these cases certain standards were adopted arbitrarily. The ability to walk without aid of a cane or crutches and the possession of a practical range of painless motion of the hip were selected as the criteria of the good result. A practical range of motion of the hip was considered to be that range of motion which allowed the patient to carry on normal activity without undue restriction or encumbrance. The ability to tie the shoe on the foot of the affected leg and to climb the stairs one foot ahead of the other in the normal manner were often used to determine the practical range of motion.

If the patient was able to get around with the help of a cane, and pain and limitation of motion of the hip were slight, the result was considered to be fair. If the patient derived no benefit from the operation or was worse after the operation than before, the result was classed as poor and considered a failure.

Eight of the seventy one cases were discarded because follow up observation was not adequate enough to enable us to evaluate the results finally. Therefore, sixty three cases (88.7 per cent of the total) are left for analysis. The results are given in Table IV.

TABLE IV END RESULTS OF 63 BRACKET OR MODIFIED BRACKET OPERATIONS

RESULT	CASES	PER CENT
Good	42	66.6
Fair	9	14.3
Poor	11	17.5
Death	1	1.6
Total	63	100.0

Evaluation of results for the entire series according to the method of internal fixation used is given in Table V. The increasing use of vitallium screws as the means of fixation of choice is obvious.

TABLE V END RESULTS ACCORDING TO FIXATION USED

MEANS	PATIENTS		RESULTS CASES			
	TOTAL	NOT TRACED	GOOD	FAIR	POOR	DEATH
Vitallium screws	44	2	31	4	-	0
No fixation	10	4	3	3	2	0
Beef bone screws	4	1	3	0	0	0
Wire nail	3	1	0	1	0	1
Steel nail	2	0	0	1	1	0
Johannsen nail	1	0	0	0	1	0
Knowles pin	1	0	1	0	0	0
Total	71	8	42	9	11	1

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and the acetabulum was noted. Finally one case was judged to be a failure because pain persisted after the operation.

COMMENT

The end results of various operative procedures that have been reported in the literature in the last few years are summarized in Table VI.¹⁴ The criteria on which these end results have been judged may vary widely but it seems evident that, in the hands of experienced surgeons in a large series of cases of nonunion of the neck of the femur, repaired by any one of the several procedures now being used, favorable results can be expected in from 60 to 80 per cent. Good or fair results were obtained in about 80 per cent of our entire series.

Although the Magnuson modification of the Brackett operation is a somewhat more complicated surgical procedure than for instance the osteotomy it is still our opinion that the good results obtained by this operation are so much better than the good results obtained with other reconstructive procedures that its continued and increasing use is justified. The prerequisites are not as stringent as for bone grafting procedures and the modified Brackett operation is applicable in a large majority of cases of nonunion in which the head of the femur is viable. The operation should not be attempted of course in the presence of articular damage. Age in itself is not a criterion in the selection of cases. Twenty seven of our seventy-one patients were in the sixth or seventh decade.

Since the predominant cause of failure was slipping of the shaft from the head careful positioning at the time of operation must be emphasized. As much valgus as possible must be obtained and the fragments must be transfixed adequately. In only one case in this series was there a persistent abduction deformity and that was not sufficient to interfere markedly with full function.

SUMMARY AND CONCLUSIONS

The need for careful collection and study of end results obtained with the various operative procedures designed for the restoration of function in united fractures of the femoral neck continues. As an aid in this study a well defined set of criteria should be adopted to standardize the evaluation of end results by different authors.

At the Mayo Clinic the Brackett operation or the procedure as modified by Magnuson was used in seventy-one cases of nonunion after fracture of the femoral neck in the years 1920 to 1941 inclusive. Good results were obtained in 66.7 per cent of the sixty-three cases in which evaluation was possible.

Internal fixation by means of beef bone screws or metallic nails or screws was used in fifty-five of the seventy-one cases and good results were obtained in thirty-five. In four of these fifty-five cases follow up data were not adequate to allow evaluation.

Proper selection of cases, careful operative work, valgus position of the femoral head on the remodeled shaft and adequate internal fixation are important in this operation.

as pentobarbital is given by mouth Ten to twenty minutes before administration of the spinal anesthetic 20 mg of desoxyephedrine (Methedrine or Drinalfa) are injected intramuscularly in most cases This agent has been found to be more efficacious in preventing blood pressure fall than the usual 50 mg of ephedrine " "

The spinal anesthetic solution is made up by mixing dry tetracaine (pontocaine nuphanoid) in 10 per cent dextrose so that 1 c c of solution contains 10 mg of pontocaine The dose of pontocaine varies from 3 to 10 mg so that 0.3 to 1.0 c c of the pontocaine in dextrose solution is taken up into a syringe To this is added 1 c c of ephedrine sulfate containing 50 mg of the salt The total volume of the mixture will thus be between 1.3 and 2.0 c c No spinal fluid or other diluent is added as a reasonably concentrated hyperbaric solution is desired

The patient is then placed in the lateral position on the affected side The spinal puncture is made as rapidly as possible since lying on the affected side is painful and the spinal anesthetic solution is injected very slowly over a period of two minutes by the clock The operating table is level and is kept this way for at least ten minutes after completion of the injection He may then be positioned for surgical convenience An intravenous infusion of saline or glucose solution is usually started to which blood or plasma may be connected for later use Weighting the pontocaine with dextrose is necessary to make the anesthetic solution heavier than spinal fluid Thus gravity carries more of it to the dependant half of the dural sac where it bathes the roots of the nerves supplying the affected leg A small volume increases hyperbaricity and minimizes dispersion during injection Slow injection also decreases dispersion The ephedrine lengthens the time required for fixation of the spinal anesthetic solution so that a minimum of ten minutes is required but this is more than compensated for by the increase in total duration which it provides

This attempt to concentrate the solution around the nerve roots of the affected side makes a smaller dose produce more complete and longer lasting anesthesia Since the leg thigh and buttock are innervated by the first lumbar to the second sacral spinal segments an injection at the third or fourth lumbar interspace will reach all nerve roots concerned with a minimum of dispersion

RESULTS

In all sixty seven cases the anesthesia was satisfactory in speed of onset and in producing complete relaxation of the large muscles about the hip The unaffected leg could be freely moved throughout the operation in most cases although some paresthesia was usually present in it

In Table I it is shown that in cases lasting less than 1½ hours the duration was sufficient in all cases with or without ephedrine added to the anesthetic mixture However in cases lasting more than 1½ hours the prolongation relieved with ephedrine is evident Table II shows the two cases out of thirty four lasting more than ninety minutes in which ephedrine was used where supplementary anesthesia was required and the two cases out of eight

PROLONGED SPINAL ANESTHESIA FOR OPERATIONS ON THE HIP AND LOWER EXTREMITY

J EUGENE RUBEN MD PHILADELPHIA PA

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THE question of anesthesia for the elderly patient about to undergo reduction of a fractured hip or amputation of a gangrenous leg is always a difficult one. Problems in a large city hospital are the poor general condition of the patients and, in many cases, old age. In addition there are the complications of frequent fluoroscopic reduction with the automatic removal from consideration of all hydrocarbon agents that goes with this procedure and the indefinite duration of the operation itself. This depends on technical difficulties and cannot be forecast. For these reasons we began in June 1946 to use a concentrated solution of pontocaine dextrose ephedrine for unilateral spinal anesthesia in a search for a workable routine which would satisfy surgical requirements, remove the explosion hazard and provide a reasonably safe anesthetic method. Our study covers all operations for fractured hip done between June 1 and November 30, 1946, and includes some other operations confined to one lower extremity done under this technique. There were sixty-seven cases studied during the six month period.

The idea of using vasoconstricting drugs intrathecally is not new and was described in the early part of this century. In 1943 Romberger¹ mentioned mixing ephedrine with procaine, more recently Prickett, Gross and Cullen² and Potter and Whitacre³ have reviewed the literature and reported clinical studies in which vasopressor drugs were administered subdurally. These recent reports indicate that there is prolongation of anesthesia with equal or smaller doses of spinal anesthetic agents and no increase in complications during or after anesthesia.

Unilateral spinal anesthesia is familiar to all who have seriously interested themselves in spinal anesthesia. Maxson⁴ stated: "It is quite possible to secure anesthesia much more intense on one side than the other and of longer duration by keeping the patient motionless for several minutes. True unilateral anesthesia has not occurred in the writer's experience but it could be produced if any advantage were to be gained thereby."

The purpose of this paper is to present a technique for selected unilateral cases in which it is felt that a definite advantage is gained by unilateral spinal anesthesia prolonged by the use of vasopressor drugs intrathecally.

TECHNIQUE

When premedication is indicated, morphine and scopolamine are administered hypodermically ninety minutes before operation in the proportion of 25 parts of morphine to 1 of scopolamine or a rapidly acting barbiturate such

TABLE III DEATHS WITHIN THIRTY DAYS OF OPERATION

CASE	NAME	SEX	AGE	PROCEDURE*	ANESTHETIC		DEATH		
					PONTOCAINE (MG)	ETHEDRINE (MG)	TIME†	CAUSE	TIME P O
1	E S	F	66	Osteotomy of hip	8	50	185	Congestive failure (P)	7 days
4	M L	F	77	Open reduction of hip	7	50	135	Multiple pulmonary emboli (P)	7 hr
5	B M	F	78	Open reduction of hip	5	—	130	Bronchopneumonia, gangrenous cystitis (P)	10 days
6	A A	M	71	Open reduction of hip	5	50	145	Hemorrhage from gastric ulcer (P)	20 days
9	C R	F	92	Closed reduction of hip	5	25	75	Pulmonary embolus	15 days
15	S R	M	84	Closed reduction of hip	7	50	70	Pulmonary embolus (P)	10 days
34	M F	F	63	Closed reduction of hip	10	—	110	Bronchopneumonia	9 days
38	A U	M	85	Open reduction of hip	5	—	115	Bronchopneumonia, congestive failure (P)	18 days
39	F J	F	79	Closed reduction of hip	4	—	110	Bronchopneumonia (P)	21 days
40	A B	F	97	Closed reduction of hip	3	—	80	Bronchopneumonia	25 days
45	M F	F	80	Open reduction of hip	5	50	85	Pulmonary embolus (P)	4 hr
47	T B	M	89	Open reduction of hip	5	50	160	Inanition and urinary complication	23 days
52	H H	M	83	Open reduction of hip	5	—	80	Pulmonary embolus (P)	4 days
56	B B	F	76	Mid thigh amputation	3	50	30	Uremia, diabetes	8 days
67	A K	F	73	Open reduction of hip	10	50	135	Bronchopneumonia (P)	19 days

*All open reductions had Neufeld nail or Thornton plate with Smith Petersen nail all closed reductions had insertion of Smith Petersen nail

†Time in minutes from spinal injection to completion of operation (P) Indicates findings confirmed at post mortem examination

thrombosis existed before operation was started. Neither had blood pressure drops of any consequence during operation. Of the other three such deaths only one (Case 9) had a marked fall in blood pressure during operation, and since she survived fifteen days, we do not feel the spinal anesthetic and its accompanying blood pressure fall were necessarily responsible for the embolus. In none of the cases in this series was prophylactic or therapeutic vein ligation performed. *Bronchopneumonia was the primary cause or a complicating factor in six deaths.* Only two other cases of bronchopneumonia occurred in the series. Seven of the eight cases of bronchopneumonia encountered occurred in patients over 70 years of age and the eighth case was a man of 63 years. Only one patient complained of headache following spinal anesthesia, but the aged usually complain less.

In Table IV are given data on ten of the longer cases in the series, all of which survived. The anesthesia records of two of these patients are shown in Figs 1 and 2. The level blood pressure and relatively stable pulse rate in Cases 54 are illustrative. In Case 30 (Fig 2) the pulse and blood pressure

of similar duration where it was not used which required a supplement. The longest case (Case 30) in the series was a hip osteotomy lasting three hours and thirty five minutes under 10 mg of pontocaine with 50 mg of ephedrine in a muscular 36-year old man. He required no supplement, and volunteered that the pain did not appear for two hours after operation was completed. He had completely unilateral anesthesia.

TABLE I COMPARISON OF PONTCAINE DEXTROSE WITH AND WITHOUT 50 MG EPHEDRINE SULFATE INTRATHECALLY

	SATIS- FACTORY	SUP- PLEMENT	AVERAGE DURATION
With ephedrine			
Less than 90 minutes	18	0	70 minutes
More than 90 minutes	32	3	135 minutes
Without ephedrine			
Less than 90 minutes	7	0	67 minutes
More than 90 minutes	6	2	130 minutes

Sixteen of the procedures were closed reductions of hip fractures done under fluoroscopic guidance. The anesthesia was of such duration in these cases that not even the addition of morphine was necessary. The smallest doses of pontocaine were used in these patients.

There were no immediate or postoperative complications attributed to the anesthesia by surgeons or anesthesiologists. No postoperative atelectases occurred, which is especially notable since thirty seven of the sixty seven patients (55 per cent) were more than 70 years old. No cases of nerve root damage or irritation were encountered.

Altogether fifty two patients were given intrathecal ephedrine and in fifteen it was omitted. Table III shows that there were nine deaths among the fifty two patients who received ephedrine and six deaths among the fifteen who did not.

Five of the fifteen deaths were due to pulmonary emboli. Two of these occurred within seven hours of operation and it is presumable that phlebo-

TABLE II CASES REQUIRING SUPPLEMENTARY ANESTHESIA

CASE	NAME	SEX	AGE	PROCEDURE	ANESTHETIC		TOTAL TIME (IN MIN.)*	SUPPLEMENT		RE MARKS
					PONTO- CAINE (MG.)	EPHE- DRINE (MG.)		AGENT	TIME AFTER SPINAL (MIN.)	
8	J M	M	50	Triple arthrodesis of ankle with ten toes transplant	0	50	1 0	Al- liron ether	100	Pain from tourni- quet
19	S F	F	63	Open reduction of hip with nail and plate	50	50	1 50	Cyclo- pro- pane	70	
33	M K	F	25	Osteotomy of hip	150	0	1 5	Pento- thol	90	
36	A C	F	63	Open reduction of hip with nail and plate	50	0	1 0	Cy- clo- pro- pane	90	Psy- chotic poison

*Time from injection of spinal anesthetic solution until completion of operation including cast, if any.

TABLE III DEATHS WITHIN THIRTY DAYS OF OPERATION

CASE	NAME	SEX	AGE	PROCEDURE*	ANESTHETIC		DEATH	
					PONTO CAINE (MG)	EPHED RINE (MG)	TIME†	CAUSE
1	E S	F	66	Osteotomy of hip	8	50	185	Congestive failure (P)
4	M L	F	77	Open reduction of hip	7	50	135	Multiple pulmonary emboli (P)
5	B M	F	78	Open reduction of hip	6	-	130	Bronchopneumonia, gangrenous cystitis (P)
6	A A	M	71	Open reduction of hip	5	50	145	Hemorrhage from gastric ulcer (P)
9	C R	F	92	Closed reduction of hip	5	25	75	Pulmonary embolus
15	S R	M	84	Closed reduction of hip	7	50	70	Pulmonary embolus (P)
24	M F	F	63	Closed reduction of hip	10	--	110	Bronchopneumonia
38	A U	M	85	Open reduction of hip	5	-	115	Bronchopneumonia, congestive failure (P)
39	F J	F	79	Closed reduction of hip	4	--	110	Bronchopneumonia (P)
40	A B	F	97	Closed reduction of hip	3	--	80	Bronchopneumonia
45	M F	F	80	Open reduction of hip	5	50	85	Pulmonary embolus (P)
47	T B	M	89	Open reduction of hip	5	50	160	Infection and urinary complication
52	H H	M	83	Open reduction of hip	5	--	80	Pulmonary embolus (P)
56	B B	F	76	Mid thigh amputation	3	50	30	Uremia, diabetes
67	A K	F	73	Open reduction of hip	10	50	135	Bronchopneumonia (P)

*All Open reductions had Newfeld nail or Thornton plate with Smith Petersen nail all closed reductions had insertion of Smith Petersen nail

†Time in minutes from spinal injection to completion of operation (P) Indicates findings confirmed at post mortem examination

thrombosis existed before operation was started. Neither had blood pressure drops of any consequence during operation. Of the other three such deaths only one (Case 9) had a marked fall in blood pressure during operation, and since she survived fifteen days, we do not feel the spinal anesthetic and its accompanying blood pressure fall were necessarily responsible for the embolus. In none of the cases in this series was prophylactic or therapeutic vein ligation performed. Bronchopneumonia was the primary cause or a complicating factor in six deaths. Only two other cases of bronchopneumonia occurred in the series. Seven of the eight cases of bronchopneumonia encountered occurred in patients over 70 years of age and the eighth case was a man of 63 years. Only one patient complained of headache following spinal anesthesia, but the aged usually complain less.

In Table IV are given data on ten of the longer cases in the series, all of which survived. The anesthesia records of two of these patients are shown in Figs 1 and 2. The level blood pressure and relatively stable pulse rate in Case 54 are illustrative. In Case 30 (Fig 2) the pulse and blood pressure

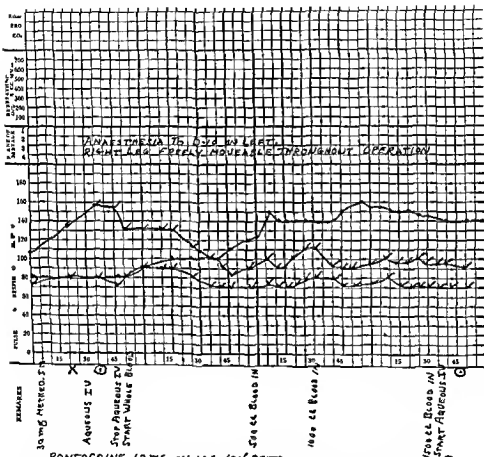
No. 30
 Ward MEN'S ORTHO
 Name HOWARD L.

PHILADELPHIA GENERAL HOSPITAL
 ANESTHESIA RECORD

DATE July 12, 1946

PS 0 2 3 4 5 6 7

Age 36 O.R. F



PONTOCAINE 10 mg in 1 cc 10% DEXTROSE
 Agals. PLUS 50 mg PINEBARINE SULPHATE in 1 cc 10% DEXTROSE
 Operation OSTEOPLASTY, LEFT HIP FOR CORRECTION OF FRACTURE
 DEFORMITY SECONDARY TO BULLET WOUND
 Surgeon DR. N. B. K. AND G.
 Anesthetist DR. R.

FIG. 2—Anesthesia record Case 30

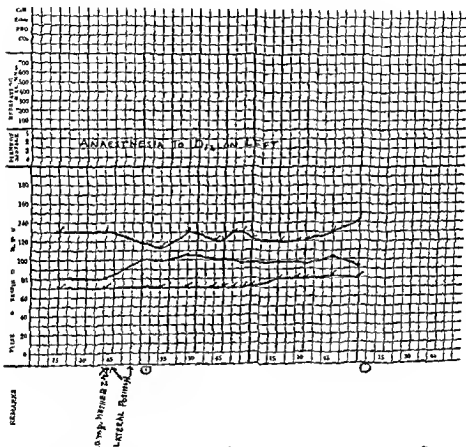
Page 54
Ward W ORTHO

PHILADELPHIA GENERAL HOSPITAL
ANESTHESIA RECORD

DATE NOV 24 '46
 PG 3 3 ① 4 3 4 3

NAME - GRACE H--

Age 70 Sex G



PONTACINE, 5MG IN 0.5CC 10% DEXTROSE
AND 50MG EPHEDRINE SULFATE - Tabloid LEFT SPINAL
CLOSED REDUCTION OF LEFT INTRACAPULAR HIP FRACTURE
AND INSERTION OF SMITH-PIEDERSON NAIL - FLUOROSCOPIC GUIDANCE
DAS LAND B.
DR. K. -

prolonged periods of darkness make adjustments of gaseous anesthetic mixtures difficult, that this method of spinal anesthesia is a positive, relatively simple technique with a wide margin of safety

SUMMARY

1 A method for prolonged unilateral spinal anesthesia with pontocaine dextrose ephedrine mixture is described

2 The application of the method in prolonged operations on the hip and lower extremity in the old, poor risk patient is discussed

3 The method has particular value in manipulations of fractures where the duration cannot be forecast and the majority of the operation is done in the dark under the fluoroscope

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the
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TABLE II PERTINENT DATA ON TEN ILLUSTRATIVE CASES, WITH NO DEATHS

					PRESSOR	PONTO CAINE	REMARKS INCLUDING OPERATIVE AND P O
				tion of hip	mg I M		spontaneous recov- ery, bronchopneumo- nia 4th day
14	G W	M	78	Hip spica after fail- ure to place 9 P nail	Method 20 mg I M	7	155
17	G O	F	75	Open reduc- tion of hip	Drinalfa 10 mg I M ephed 25 mg I V	7	150
18	G F	M	69	Open reduc- tion of hip	Method 20 mg I M	7	145
23	F V	M	58	Open reduc- tion of hip	Ephed 25 mg IV	8	170
29	E S	F	66	Osteotomy of hip	Ephed 25 mg IV	8	180
30	H L	M	36	Osteotomy of hip	Method 30 mg I M	10	215
54	G H	F	70	Closed reduc- tion of hip	Method 20 mg I M	5	160
66	B K	F	51	Open reduc- tion of hip	Method 20 mg I M	6	125

*All open hip reductions had Neufeld nail or Thornton plate with Smith Petersen nail
 †All closed hip reductions had insertion of Smith Petersen nail

†Pontocaine dissolved in 10 per cent glucose with 50 mg 5 per cent ephedrine solution
 ‡Time in minutes from spinal injection to completion of operation

were maintained for the first forty five minutes of operation but the patient then went into shock secondary to hemorrhage in the form of markedly increased oozing from all surfaces in the wound

DISCUSSION

The minimal physiologic changes seen in unilateral spinal anesthesia are thought to be due in part at least to unilateral rather than the usual bilateral sympathetic paralysis. Less difficulty with voiding postoperatively is noted probably due also to the unilateral paralysis. Unilateral anesthesia cannot be obtained with the continuous spinal technique of either Lemmon⁷ or Touhy.⁸ The single dose method is simpler to induce and obviates the difficulties of maintaining needle or catheter position during operation.

It is not felt that this spinal method is superior to good inhalation anesthesia for operations done in the light. But it is felt that for those cases done under fluoroscopic guidance where explosive agents cannot be used, and where

bold incision, deepened abruptly without first elevating the skin margins, could easily sever one of these lymphatics. The excision of an overlying lymph node, which obstructed the field of operation, could tear some of these tiny channels even with careful dissection and without recognition of the injury at the time. Dennis³ is to be credited with the observation, made during a high femoral ligation, of "a small spurting vessel. It spurted a colorless clear liquid, not blood, and it was ligated."

Lymph clots more slowly than blood and is lower in protein content.^{4,7} In proportion to its protein content, lymph contains less of the coagulation factors than blood plasma. The protein content of the peripheral lymph from a dog's leg is only one fourth of the normal serum protein, 1.66 to 6.59 per cent.⁶ It should not be unfair to assume that fibrinogen is materially and possibly proportionately reduced, although there are no available quantitative values for peripheral lymph fibrinogen. The viscosity of lymph is less than that of blood serum and varies directly with its protein content.

Howell⁷ has shown that delayed clotting is due to lack of thromboplastic material. In the blood this substance is contributed chiefly by the platelets and to a minor degree by the leucocytes. In lymph, platelets are lacking, and the white cells are poor sources of thromboplastin. Howell also stated that lymph contained a relative excess of antithrombin. The delay in the clotting of lymph may be due to lower viscosity, lower protein content, lower fibrinogen content, lack of thromboplastin, excess of antithrombin, or more likely a combination of these factors.^{4,6}

I have encountered three instances of lymph leakage after saphenous vein ligation. The first occurred in one of my own patients, a middle aged Negro, with varicosities and recurring ulceration confined to one leg, which had begun many years before as a phlebitis complicating typhoid fever. Four days after ligation a swelling appeared beneath the incision, which when opened poured out an estimated 300 c.c. of clear lymphlike fluid. The leak persisted for three weeks, finally subsiding after repeated packing and tight bandaging, while the patient was ambulatory. At operation, three adherent lymph nodes overlying the saphenous bulb were retracted too vigorously.

A second case came to my attention, occurring in a middle aged white woman whose varicose veins were the site of an acute phlebitis. The left saphenous vein was ligated without retrograde injection, and five days later a painful swelling appeared beneath the operative scar, which, when incised, drained lymph (clear serum). This leak lasted for two months with intermittent drainage of lymph, described in the record as clear and of a serous nature and finally the recurrent swelling was explored, revealing a thin walled cyst filled with two ounces of clear opalescent fluid. The cyst wall was curetted and the wound packed wide open with gauze. The wound drained lymph for almost one month and then healed. This case also illustrates the greatly augmented lymph flow associated with phlebitis.

A third instance occurred in a white man, one week after saphenous vein ligation and retrograde injection with sodium morrhuate. A swelling at the site of operation was then incised with the escape of 75 c.c. of clear lymphlike fluid. The fluctuant tumor recurred after repeated drainages over a period

LYMPH LEAKAGE (LYMPHORRHEA)*

A COMPLICATION OF SAPHENOUS VEIN LIGATION, WITH SUGGESTIONS FOR TREATMENT

F C FISHBACK MD WASHINGTON D C

IT IS amazing that lymph leakage should be so unusual a complication in view of the frequency of saphenous vein ligations the propinquity of the sub inguinal lymphatics and nodes to the saphenofemoral junction and the slow clotting of peripheral lymph. The treatment of varicose veins by high saphenous vein ligation with or without retrograde injections has become one of the commonest of all surgical procedures. Perilymphangitis may be present and the lymphatics swollen and engorged with lymph. In these circumstances a tear in the wall of a lymphatic would produce an unrecognized lymph leak which might persist.

Harkins and Schug¹ have described a single instance of lymph leakage after saphenous vein ligation. At operation they noted "a large adherent overlying lymph gland", a lymph leak appeared a few days later and persisted for three months. The disaster following injury to the thoracic duct frequently referred to in surgical texts is due chiefly to the lack of clotting qualities in the chyle. Reference to lymph leakage after femoral vein ligation is rare² even though the operation involves deeper dissection and wider retraction than the much more common procedure of saphenous vein ligation.

The lymphatics of the leg consist of two sets: superficial and deep each following the veins closely in distribution. The superficial lymphatics lie subcutaneously in the superficial fascia running in three trunks one following the course of the long saphenous vein another along the short saphenous vein and a third arising in the gluteal region. The internal lymphatic trunks which follow the long saphenous vein are three or four in number and arise from a plexus on the dorsum of the foot and drain the toes sole and both borders of the foot. The external trunks, which parallel the short saphenous vein are two or three in number arising in the region of the heel and posterior half of the outer edge of the foot and enter the internal trunks which terminate in the superficial lymph nodes. This group of nodes lies beneath the superficial fascia in Scarpa's triangle. These nodes are large vary in number from ten to twenty and may be divided arbitrarily into a superior and inferior group by a horizontal line through the saphenous opening. The inferior group of subinguinal lymph nodes is placed on either side of the upper end of the long saphenous vein and drains the efferent lymphatics from the lower leg as well as those from the genitals perineum and buttocks.

It is these subinguinal nodes and the superficial lymphatics coursing along the saphenous vein which are most likely to be torn in the dissections of the saphenofemoral junction. These lymphatics are small friable and lack the protective coloring of veins. Vigorous displacement of an overriding lymph node by a retractor might easily rupture one of these small lymph vessels. A

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*Neither lymph leakage nor lymphorrhea are mentioned in the Quarterly Cumulative Index Medicus.

Case Reports

MAXILLARY TUMOR OF RETINAL ANLAGE

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The School of Medicine of the University of Oklahoma)*

HEREIN is reported a benign neoplasm removed from the maxilla of a 6 month-old infant and composed of tissue elements of the retina. This is believed to be the first such growth ever recorded.

REPORT OF CASE

A 6 month old white female child was admitted to the University of Oklahoma Hospitals, Oklahoma City, March 1, 1946, with a firm mass protruding from the hard palate. The mother, 23 years old, stated that the patient was her second child, born after an uneventful pregnancy, at term, with no complications of labor or of delivery. At birth the child weighed 8 pounds and presented no abnormalities. Development was unimpaired and she was apparently perfectly well until December, 1945. At this time, when about 4 months old, she fell and struck the upper lip, over which a blue streak appeared. The next day the area became swollen to such an extent that the physician incised the lip from the inside of the mouth. Bright red unclotted blood was obtained. This reduced the size of the lip temporarily.

On admission to the hospital the child was well developed, well proportioned, well nourished, and in apparent good health. The upper lip was blue and somewhat swollen and distorted. A nontender, firm mass, about 5 cm in diameter, protruded into the mouth over the anterior portion of the right maxilla distorting the right side of the upper lip. The mass appeared to be attached to the bone. The overlying mucosa of the palate and gums was intact. Other physical findings and examination of the blood and urinalysis were essentially negative. Roentgenographic examination of the face disclosed a soft tissue tumor in the right anterior maxillary region with displacement of the teeth (Fig 1). The heart was of usual size, shape and position. The lung fields were clear.

On March 8, 1946, under endotracheal ether anesthesia, the right external carotid artery was ligated. An elliptical incision was then made through the mucous membrane of the mouth and periosteum directly over the mass. The soft tissues with the periosteum were elevated. The alveolar process was divided medially and laterally to the tumor, after which the tumor shelled out without difficulty. The bleeding areas in the bone were controlled with bone wax, the roof of the mouth was reconstructed and the space packed with sulfanilamide ointment gauze the end of which was brought out through the medial end of the incision just behind the lip. Ophthalmoscopic examination March 14 1946 disclosed no visual disturbances and no changes in the eye grounds. The patient made an uneventful recovery and with the wound completely healed.

on Nov 14 1946

no recurrence of it

no deformity of the mouth and face (Figs 2 and 3)

The specimen consisted of a globular, somewhat lobulated firm mass, 5 by 3 by 3 cm, weighing 25 Gm. Part of the surface 4 by 3 cm., was covered by a smooth membrane, the remainder appeared raw. There were four teeth: two incisors, one canine, and one premolar.

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of nine months, at which time the wound was explored and a sac containing the same lymphlike fluid was excised. Recurring swelling and lymph leakage persisted another five months at which time the original incision was laid wide open and packed and bandaged tightly with subsequent healing. This is the only case in which a retrograde injection was done.*

There are several effective means of treatment. Obviously injury to the thin walled lymphatics would not occur if they carried a colored fluid to facilitate their identity. The application of an elastic pressure bandage from the foot to above the incision, with elevation of the leg, will invariably stop the leak within a short time due to forcible collapse of the lymphatics and resultant slowing of the lymph flow to a rate at which clotting can occur. If the wound is laid open or if it disrupts from distention with lymph, firm packing of the wound beneath an elastic bandage will plug the leak and hasten clotting. The local application or injection of any thromboplastic material such as Thrombin Topical† should cause clotting by affording a surplus of thromboplastin in the subcutaneous tissues about the leak. Such an injection is not without danger.

Lymph will continue to leak from a torn lymphatic because it is too low in all the factors of coagulation to make a substantial clot. Drinker⁵ has suggested not only that the lymphatic fibrinogen is low, but also that the fibrinogen in the subcutaneous tissues about the leak may fail to participate in the clotting process unless there is an excess of thromboplastic material present to bring about a coagulum of better quality. What he terms a rather crude though effective method of accomplishing this consists of crushing the subcutaneous tissues with the jaws of a hemostat in the region of the leak thereby releasing excess tissue juice or extract which is high in thromboplastic material in the immediate vicinity of the fistula. Such a procedure would be attended by some danger of infection unless careful asepsis were observed.

These therapeutic suggestions are offered because of the possibility of this exceedingly annoying complication of the everyday procedure of saphenous vein ligation. That this complication has been barely mentioned before can be attributed either to its rarity or more likely to its being regarded as of minor importance. No matter how trivial anything that can be so annoying both to patient and doctor deserves both recognition and prompt relief.

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*I am grateful to Dr. Paul Potekil and Dr. Samuel Zola for their permission to cite their cases.

†Manufactured by Parke Davis & Company, Detroit, Mich.

The cut surfaces were smooth and slate black, streaked with gray white (Fig 4). The mass was bordered partly by a delicate bony plate, 0.1 to 0.3 cm thick, and partly by a connective tissue capsule 0.2 cm thick.

Microscopic preparations, stained with hematoxylin and eosin, and representing many parts of the specimen, disclosed various sized spaces lined with cuboidal cells. These contained brown or dark brown granules frequently obscuring the nucleus. In occasional lumina there were coarse infoldings resembling the eiliary processes of the eye (Fig 5). In intimate contact with the lumina and also elsewhere there were sheets and nests of deeply stained round or oval nuclei with practically no cytoplasm and some fibrils (Fig 6). All these cells were within a delicate fibrillar ground substance containing round or elongated vesicular nuclei with

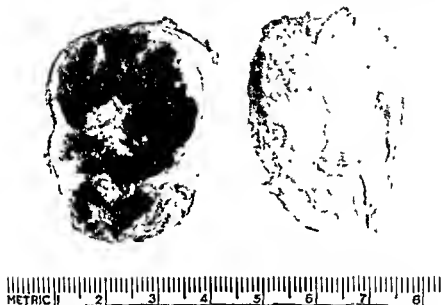


Fig 4.—The specimen removed is a globular mass apparently encapsulated weighing 23 Gm. The cut surfaces are smooth and slate black streaked with gray-white.

hardly discernible cytoplasm fading into the fibrils. The fibrils in the stroma in places were neat and delicate such as are usually seen within nerves or in the perineurium. Elsewhere there were collagenous bundles. In a preparation including the smooth surface there was a broad layer of stratified squamous epithelium with broad spinous and keratinized layers. The line between the squamous epithelium and the subjacent connective tissue was perfectly straight. In the deeper layers there were strands of epithelium composed of two rows of cell nuclei. Further inward there was a row of columnar cells in palisade arrangement, then cells with stellate processes in a light fibrillar ground substance. There were also occasional islands of osseous tissue. This zone merged with the connective tissue stroma of the spaces lined with cuboidal cells.

COMMENT

The spaces lined by cuboidal cells containing brown granules with their patterns of infoldings mimicked the eiliary processes of the eye. The sheets of almost naked cell nuclei resembled the nuclear layers of the retina or the cells seen in neuroblastomas. These microscopic appearances left no doubt that the principal component of the neoplasm was derived from cells of retinal



Fig 1



Fig 2



Fig 3

Fig 1—Soft tissue tumor in the right anterior maxillary region with displacement of the teeth.

Figs 2 and 3—Eight months after removal of the growth there was no recurrence. The two sides of the maxilla are symmetrical and there is practically no deformity of the mouth and face.

anlage The benign character of the neoplasm was obvious since the tissue elements were in orderly relation to one another and no obvious activity of multiplication of the cells was seen Furthermore the tumor was well encapsulated and did not invade adjacent structures The size of the neoplasm however, suggested that it had a growth potentiality similar to that of the individual Had it not been removed the neoplasm probably would have enlarged progressively with the growth of the child

SUMMARY

The clinical history is presented of a 6 month old white girl who had a tumor removed from the maxilla The neoplasm composed of tissue elements of the retina is believed to be the first tumor of retinal anlage ever recorded

FIG 5



FIG 6

anlage The benign character of the neoplasm was obvious since the tissue elements were in orderly relation to one another and no obvious activity of multiplication of the cells was seen Furthermore the tumor was well encapsulated and did not invade adjacent structures The size of the neoplasm however suggested that it had a growth potentiality similar to that of the individual Had it not been removed the neoplasm probably would have enlarged progressively with the growth of the child

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PERFORATION OF THE AORTA BY ACID GASTRIC CONTENTS AT SITE OF GASTROESOPHAGOSTOMY

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PERFORATION of the thoracic aorta is not common, but does occur from time to time, as reports in the medical literature indicate. In general when perforation takes place, it is caused by foreign bodies such as fish bones or pins in the esophagus, bullet wounds, or neoplastic invasion of the aortic wall from an esophageal cancer. Isolated instances of perforations of the thoracic aorta by penetrating peptic ulcers of the esophagus have been reported by Christopher son,¹ Eversmann,² and Flower.³ Dash⁴ described a case of fatal hemorrhage from perforation of the abdominal aorta by a chronic ulcer of the third portion of the duodenum. Because of its unique nature the following case seems worthy of reporting.

A 59 year old farmer entered Albany Hospital in September, 1945, with one year's history of indigestion, anorexia, epigastric pain, thirty pounds' weight loss, and no response to an ulcer regime. A gastrointestinal series was reported in part as follows: "A liquid barium passes down the esophagus, its progress is temporarily arrested at the cardiac end of the stomach by cardiospasm. There are no visible ulcerations or new growths." He was discharged on Sept. 30, 1945, to be followed by a gastroenterologist.

The symptoms steadily increased in severity and in addition he had frequent bouts of nausea and vomiting immediately after eating or drinking. He was readmitted on April 25, 1946, at which time roentgenographic studies of the gastrointestinal tract revealed a filling defect in the cardiac end of the stomach, toward the lesser curvature, consistent with a gastric neoplasm. The tumor also involved the distal portion of the esophagus.

On May 9, a large, ulcerated, granular mass 4 by 2.5 by 1.5 cm. was excised by a trans thoracic approach and a gastroesophagostomy was performed. This mass was in the lesser curvature of the gastric fundus and extended into the submucosa of the distal esophagus. The spleen and tail of the pancreas were also resected. The specimen was reported pathologically as an infiltrating adenocarcinoma, grade II, of the cardiac portion of the stomach invading the submucosa and muscularis of the adjacent esophagus. The upper end of the esophagus was free of tumor. The spleen and pancreas were negative.

On May 14, a massive left sided pleural effusion was found. May 16, he became markedly distended and the abdominal incision broke down. It was resutured with stainless steel on May 18. Thoracentesis fluid on May 23 contained milk curds and suggested a leak in the anastomosis with drainage of gastric contents into the left pleural cavity. Thoracotomy was done on May 24 and again gastric contents were identified in the pleural exudate. On May 29 jejunostomy was done to relieve abdominal distention and to facilitate feeding. For several days he was nursed from the left pleural cavity and cent. There was a leucocytosis of over 15,000. In spite of intensive supportive therapy he grew steadily weaker and on June 18 he suffered a massive upper gastrointestinal hemorrhage from the mouth and died three hours later.

The pertinent findings at autopsy were limited to the operative site and the surrounding organs. The esophagus, stomach, and small intestine were filled with bright red clotted blood. At the site of the gastroesophagostomy in the left pleural cavity a circular gaping defect 2.5 cm. in diameter was noted. The edges of this defect were firmly attached to the anterior wall of the thoracic aorta by inflammatory tissue through which ran a fistulous tract that extended to the aortic wall and actually penetrated its entire thickness. This tract was lined

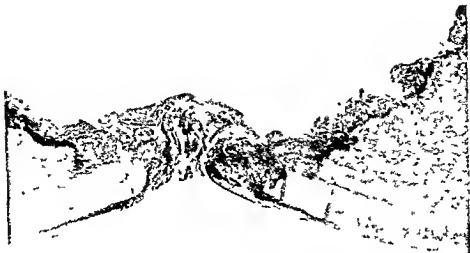


Fig 1—The perforation of the thoracic aorta is lined by granulation tissue and acute inflammatory exudate. The intima is seen at the bottom of the section and is acutely inflamed at the edge of the perforation.

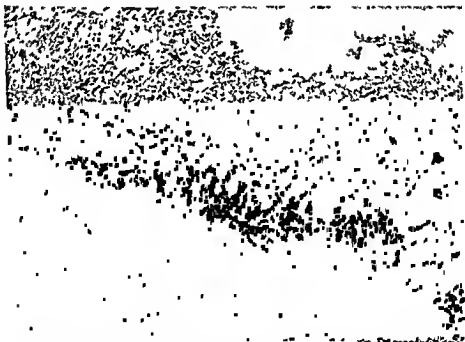


Fig 2—Section from the adventitial inflammatory mass at the junction of granulation tissue (below) and acute inflammatory exudate (above) demonstrates the coagulative necrosis commonly seen in peptic ulcers.

by hemorrhagic and blood covered inflammatory tissue. When the aorta was opened, a small perforation 3 by 1 mm. in size was found in its anterior wall. This perforation communicates with the fistulous tract through which a probe could easily be passed.

Microscopic examination of sections taken through the anastomotic site in the stomach showed extensive necrosis and chronic active inflammation on the gastric side of the anastomosis. There was no evidence of residual tumor. The distal esophagus showed only limited chronic submucosal inflammation.

A section taken through the fistulous tract at the point where it opened into the aorta showed complete destruction of the entire thickness of the aorta wall over a small area (Fig 1). The tract itself was lined by focally hemorrhagic and acutely inflamed granulation tissue. At the junction between granulation tissue and acute inflammatory exudate, a peculiar zone of coagulative necrosis, similar to that found on the base of a typical chronic peptic ulcer, was present (Fig 2).

COMMENT

This case is noteworthy because it illustrates what appears to have been a digestive, necrotizing effect of acid gastric juice on the tissues of the aortic wall. Apparently the irritating juice made its way through the periaortic soft tissues finally to erode and penetrate the entire thickness of the aorta with resulting massive hemorrhage. Particularly significant, in our opinion, is the nature of the necrosis and the inflammatory reaction for the edges of the fistulous tract leading to the aortic wall bear a striking similarity to the base of a typical peptic ulcer. There may be seen the superficial inflammatory exudate, the underlying necrotic granulation tissue, and beneath that viable and inflamed granulation tissue.

There seems to be little doubt that the aortic perforation in this instance was caused by leakage of acid gastric contents from the operative defect. No residual neoplastic tissue was found in either the stomach or esophagus and there was no evidence of new growth in or near the aorta.

Since the thoracic aorta is in such close proximity to the esophagus and appears to be susceptible to the destructive effects of the gastric juices, one might well raise the question as to the possible danger of gastroesophagostomy if postoperative leakage occurs. If it can be performed esophago-jejunostomy, where the presence of gastric juices can be eliminated might be preferable. The absence of gastric juices might well diminish the eroding, penetrating necrotizing effect of any secretions which leaked through a defect at the site of anastomosis. It is not possible for us to say with certainty that the elimination of gastric secretions would prevent such a penetrating lesion as that found in this patient. It would seem to be a reasonable deduction, however, because the nature of the necrosis and the character of the lesion suggest that the acid digestive juices played a definite role in bringing about the extensive tissue damage that resulted ultimately in erosion through the aortic wall with final fatal massive hemorrhage.

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ve-sels ligated, and the volvulus reduced. A point of complete atresia was found at one extremity of the volvulus. The bowel of the volvulus was dark, bluish red in color, and not viable. The patient was in only fair condition at this point. Administration of the anesthetic was discontinued, operative manipulation was stopped, and oxygen was given. The point of atresia and volvulus, which measured approximately 4.5 cm in length (Fig 1), was resected and a double barreled ileostomy was created. The child was then returned to the ward.

The patient's postoperative course was carefully followed by the pediatric and surgical staffs. Transfusions of whole blood were given liberally. A modified Hartman's electrolyte solution containing revitaminic acid was given intravenously in dosage according to body weight. Vitamin K was injected intravenously. The dosage of penicillin was 30 000 units every three hours. The patient was carefully observed for return of peristalsis and for the beginning of ileostomy drainage. In the late afternoon of the third postoperative day the first ileostomy movement occurred. On the morning of the fourth postoperative day, the ileostomy drainage was profuse. It had been planned to anastomose the bowel at this time and before the loss of succus entericus had created a problem of chemical imbalance. Consequently, the patient was returned to the operating room.

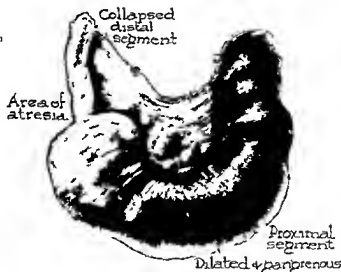


Fig 1. In infant 2 days old. A. Note gangrenous portion of the dilated proximal segment.

The proximal bowel was well decompressed. The site was resected and an open side-to-side anastomosis was performed. No. 00 gut was used in an outer row of No. 2.

Postoperatively the patient received parenteral fluids and blood transfusions. Intermittent gastric suction through a small Levine tube was applied. Peristalsis returned on the first postoperative day. On the third postoperative day the patient had a small yellow soft bowel movement. A skim milk formula and water by mouth were started. Subsequently the course was uneventful. The abdominal wound healed without infection.

The baby was followed for a period of eight months. He was active and showed normal development. He had neither gastrointestinal symptoms nor any illnesses after discharge.

TABLE I REPORTED CASES OF ATRESIA OF THE SMALL INTESTINE SUCCESSFULLY TREATED (MODIFIED FROM CORKILL AND CORKILL³)

DATE	AUTHOR	COUNTRY	SITE OF ATRESIA	OPERATION	PATIENT'S AGE (DAYS)
1911	Hockens	Holland	Mid ileal	Side to-side ileo ileos tomy	8
1916	Ernst	Denmark	Duodenal (ampulla)	Antecolic duodeno jejunostomy	11
1916	Weeks Delpont, & Buckert	U S A	Third portion of duodenum	Posterior gastro enterostomy	4
1924	Cutler	U S A	Duodenal	Anterior gastro enterostomy	4
	Porter & Carter	U S A	Duodenal	Anterior gastro enterostomy	9
1926	Stewart Sweet & Carrier	England New Zealand	Duodenal High jejunum	Anterior gastro enterostomy	9
1927	Demmer	Austria	Ileocecal	Ileocecostomy	2
1933	Corkill	New Zealand	Mid ileal	Ileostomy	
1933	Ladd	U S A	Ileal	Ileostomy followed by ileocolostomy	
	Ladd	U S A	Ileal	Ileostomy with crush ing of spur & inter closure of ileostomy	3
1943	Martin ⁴	U S A	Low ileal	Ileostomy followed by side to side ileostomy	2

SUMMARY

A case of successfully managed congenital atresia of the terminal ileum with volvulus in a newborn infant has been recorded. Initial surgical treatment was limited to resection of the proximal gangrenous loop of ileum and the segment of ileal atresia with establishment of a double barreled ileostomy. As a secondary or reparative surgical procedure, the distinctive feature of management was restoration of continuity of the ileum at the time of first ileal drainage of succus entericus on the fourth day. Systemic penicillin therapy is considered to have contributed to successful abortion of the impending peritonitis. It is suggested that the interval between initial and reparative surgical treatment could be utilized to demonstrate the absence of other areas of atresia in the defunctioned terminal ileum and colon. A similar general plan of management would appear applicable to other types of intestinal obstruction requiring resection of bowel in the infant.

The advice and assistance of Dr. Ralph V. Platou and Dr. N. Woody in the clinical management of this patient are gratefully acknowledged.

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RESECTION OF THE HEAD OF THE PANCREAS AND DUODENUM FOR MULTIPLE PANCREATIC CALCULI

JACK M. LEOPARD, M.D., AND THOMAS G. ORR, M.D., KANSAS CITY, KAN.

UNTIL recently pancreatic calculi have been treated surgically by local excision. This treatment is satisfactory when the calculi lie in the major ducts and are easily accessible. In some cases there is a diffuse involvement of the ducts or a general calcification involving a portion or all of the pancreas. In such cases partial or total pancreatectomy is necessary to eradicate the disease.

Clagett,¹ in 1946 recorded the first case of total pancreatectomy for extensive calcareous deposits involving the entire pancreas. In a discussion of resection of the head of the pancreas for carcinoma, published in August, 1946, Waugh and Clagett² mentioned a case of resection of the head of the pancreas for calcification. In November, 1946, Nuzum³ described a case of calcification of the pancreas treated by excision of the distal two thirds of the gland. In December, 1946, Whipple⁴ discussed pancreatic fibrosis associated with calcareous deposits and reported upon five patients treated by partial or complete pancreatectomy. He also included a case of total pancreatectomy reported to him personally by Zimninger.⁵ In these reports there is a total of nine cases of radical resection or excision of the pancreas to which we add one case of resection of the duodenum and head of the pancreas for multiple calculi (Table I).

CASE REPORT

J. H. R., a white man aged 45 years, was admitted to the University of Kansas Hospitals Oct. 27, 1946, complaining of upper abdominal pain.

History—For nine years this patient had episodes of upper abdominal pain which recurred about every three or four months and usually lasted from seven to ten days. The pain was of a parietal, dull type, and was relieved only by morphine. During the attacks there was anorexia and constipation but at no time was there any nausea, vomiting or jaundice. During the first attack of pain an appendectomy was done without relief. Two years before admission to this hospital an exploration was done and a mass was found in the region of head of the pancreas which was not diagnosed. During the nine year period the patient gradually lost about twenty pounds in weight.

Examination—The findings on physical examination were essentially normal with the exception of some abdominal tenderness in the epigastrium, two abdominal scars and a questionable mass which could be felt above the umbilicus. The blood amylase was 112 mg (Somogyi), blood sugar 80 mg serum by use 2 units (Terry and Lenzell) and total protein 5.3 grams. The total fat in the stool was 1.2 per cent. The tolerance test was normal. X-ray of the upper abdomen showed numerous calcified areas in the head of the pancreas (Figs. 1 and 2).

Operation—The date of the operation was Nov. 1, 1946. A transverse incision was made. Many adhesions were encountered as a result of the former operation. The pancreas was about twice its normal size and was very firm and nodular throughout its length. An effort was made to locate the stones in the pancreatic ducts without success.

It was then decided to remove the head of the pancreas. The technique suggested by Child⁶ was used for the resection (Fig. 3). The head of the pancreas, duodenum, pyloric end of the stomach, and 15 cm. of the jejunum were excised in one mass. The distal end of the jejunum was passed through the mesentery of the colon and an end-to-end anastomosis was

TABLE I SUMMARY OF RECORDED CASES OF PARTIAL OR COMPLETE PANCREATECTOMY

AUTHOR	YEAR RE- PORTED	AGE	SEX	PATHOLOGY	OPERATION	RESULTS
1 Clagett	1946	37	F	Chronic pancrea- titis with calci- fication	Total pancreatec- tomy, splenec- tomy and partial duodenectomy	Died of hypo- glycemia 2½ mo after operation
2 Vaughn and Clagett	1946	1	1	Calcification of head of pancreas	Resection of head of pancreas	1
3 Nuzum	1946	23	M	Diffuse calcifica- tion of pan- creas, cysts and fibrosis	Resection of distal two thirds of pancreas	Uneventful re- covery from operation
4 Zimninger (Whipple)	1946	39	M	Chronic pancrea- titis with pancreatic lithiasis	Total pancreatec- tomy	Died 30 hr after operation
5 Whipple	1946	42	M	Calculi in ducts and extreme fibrosis of parenchyma	Resection of head of pancreas, duodenum, 12 cm of jejunum, and antrum of stomach	Condition good 3 yr after operation
6 Whipple	1946	45	M	Calculi in ducts and chronic fibrous pancrea- titis	Resection of head and part of body of pan- creas, pylorus, duodenum, and 10 cm of jejunum	Condition good 3 yr after operation
7 Whipple	1946	45	M	Calcification and fibrosis of pancreas	Resection of duodenum, pylorus, 6 or 7 cm of jejunum, and all of pan- creas except narrow strip over mesenteric vessels	Free from pain 20 mo after operation, taking 10 15 units of in- sulin
8 Whipple	1946	26	F	Pancreatic calculi, fibrosis and dilated ducts	Total pancreatec- tomy, duodenec- tomy, pyloroc- tomy	1 yr after opera- tion in tuberculosis sanatorium, takes 84 units zinc insulin
9 Whipple	1946	46	F	Pancreatic calculi, dilated ducts, and fibrosis	Total pancreatec- tomy, duodenec- tomy, pyloroc- tomy, and splenectomy	Died on seventh postoperative day
10 Leo; and and Orr	1947	45	M	Chronic cystic pancreatitis fibrosis, and pancreatic calculi	Re-section of head of pancreas, pylorus, duo- denum and 15 cm of jejunum	Condition good 4½ mo after operation, has returned to regular occupation

made between the stump of the pancreas and the open end of the jejunum, using two rows of interrupted silk sutures. The common duct was next anastomosed to the jejunum about 5 cm. distal to the first anastomosis. This was done with an inside row of catgut sutures and an outside row of interrupted silk sutures. A gastrojejunostomy was made about 10 cm

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Follow up—After leaving the hospital this patient had an attack of fever which was apparently due to cholangitis. He recovered rapidly and returned to work seven weeks after operation. On March 15 1947 four and one half months after operation he was free from pain and working full time at his occupation.

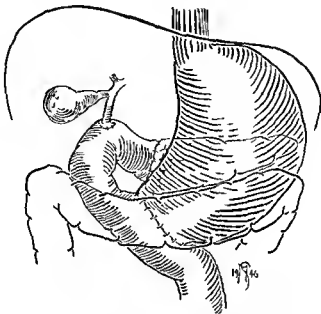


Fig 3.—Completed operation showing end to end pancreaticojejunostomy end to side choledochojejunostomy and end to side gastrojejunostomy

SUMMARY

Certain cases of extensive involvement of the pancreatic ducts with calculi or diffuse calcification of the pancreas causing intractable pain may be successfully treated by partial or complete pancreatectomy. The results thus far published indicate that both partial and complete pancreatectomy are well tolerated. The hyperglycemia resulting from complete pancreatectomy can be controlled by insulin. It is suggested that postoperative ascending biliary duct infection which sometimes develops as a result of duodenectomy may be reduced to a minimum by increasing the distance between the choledochojejunostomy and the gastrojejunostomy.

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distal to the gall duct anastomosis, using an inside row of catgut sutures and an outside row of interrupted silk sutures. The jejunum and its mesentery were sutured to the mesocolon to prevent herniation. The abdominal wound was closed with silk. A drain was passed down to the right of the common duct which emerged at the right end of the incision. This patient made a very good recovery and was dismissed from the hospital on the thirteenth postoperative day.

Pathology—Chronic cystic pancreatitis, fibrosis, and multiple pancreatic calculi were found.



Fig. 1.—Radiograph showing calculi in head of pancreas



Fig. 2.—Radiograph of resected head of pancreas

ever, because of the nuisance involved in wearing a truss and local irritation produced by it he now desired operative correction. There was a history of bleeding peptic ulcer four years previously, but now he was asymptomatic in this regard and x-ray views of the stomach and duodenum taken recently were negative. There was no other significant history.

Physical examination revealed an apprehensive slightly built adult man with no significant findings apart from the local lesion where what seemed to be a typical indirect inguinal hernia protruded through the external inguinal ring descending as far as the upper portion of the scrotum. The hernia was readily reducible and when reduced pressure upon the internal inguinal ring maintained reduction through coughing or straining. When pressure upon the internal ring was released the hernia again promptly descended into the canal and out the external ring. The possibility of an interstitial incisional hernia was considered and the right lower rectus aponeurotic scar was examined carefully with this in mind. However, no evidence of deficiency, weakness or abnormal impulse could be detected along the length of the scar which seemed solid in its entirety. Accordingly, the lesion was considered to be an ordinary indirect inguinal hernia anatomically independent of the previous operative site.

The patient was admitted to The Mount Sinai Hospital May 5, 1946 (No. 545386) and was operated upon May 6. An inguinal incision was made and the external oblique aponeurosis was incised in the direction of its fibers through the external ring. The lower leaf of the aponeurosis of the external oblique was dissected free to expose Poupart's ligament and the upper leaf retracted upward to expose the spermatic cord emerging from beneath the internal oblique muscle. The cremaster fascia was incised and the hernial sac overlying the spermatic cord anterosuperiorly was identified. The sac was opened and a nubbin of omentum which it contained was reduced into the peritoneal cavity. Traction was made upon the sac by a finger placed within it and dissection of the sac from the cord structures was proceeded with. As the dissection was carried proximally the sac was observed to diverge superomedially from the cord structures in the region of the internal ring. Moreover it was now recognized that nowhere in its extent had the sac been as closely applied to the cord structures as is ordinarily the case and a suspicion that an unusual variety of hernia was being encountered possibly an incisional interstitial hernia which had not been discernible clinically, now began to make itself felt. Further examination in the region of the internal ring revealed that the sac not only actually diverged superomedially from the cord structures at this point but that it extended as a tubular sac for a considerable distance above this level. Accordingly the internal oblique and transversus abdominis muscles were divided vertically and the sac was then easily followed in a course leading at first behind the internal oblique muscle and then behind the rectus abdominis to the lower end of the old appendectomy scar where it was seen to emerge from a deficiency in the transversalis fascia. At this point the sac was transfixed and the excess cut away. The transversalis fascia was closed over the stump. The internal oblique and transversus abdominis muscles were repaired with interrupted sutures. The cord was delivered and the transversalis fascia overlying the direct space and the internal ring were phlebotomized as there seemed to be some loss of normal tautness in these areas. The upper leaf of the external oblique aponeurosis was brought down to the shelving edge of Poupart's ligament and the lower leaf was overlapped across the suture line with subcutaneous transplantation of the cord. The skin was closed with Michel clips.

The postoperative course was entirely uneventful and the patient was discharged with primary healing on the eleventh postoperative day. He was seen for a checkup on Dec. 11, 1946 at which time he had no complaints and the wound was solidly healed with no evidence of recurrence or weakness.

COMMENT

Hernias develop interstitially when that is the least resistant path to take. Thus the ordinary interstitial inguinal hernia is most commonly found in association with an undescended testicle in which case the preformed processus vaginalis no longer leads to the scrotum and hence eliminates this as the path of least resistance. In Fisher's cases the pathway between a McBurney in

POSTAPPENDECTOMY INCISIONAL INTERSTITIAL INGUINAL HERNIA

EDWARD L. JENNIFER, M.D., NEW YORK, N. Y.

FISHER, in March, 1946, reported eight cases of postappendectomy interstitial inguinal hernia. All followed McBurney incisions, and all were "false" hernias in that none had a peritoneal sac. The herniating structure, omentum in each instance, emerged through a defect in the peritoneum of the McBurney incision and made its way under the transversus abdominis and internal oblique muscles into the inguinal canal. Thus it traversed to present at the external inguinal ring where it simulated an inguinal hernia upon clinical examination.

The following month I was visited by a patient who complained of a reducible bulge in the right groin which had appeared shortly after an appendectomy with drainage performed in 1936. On examination there was a well healed right lower rectus appendectomy scar and an independent, reducible right indirect inguinal hernia. Because of Fisher's recent article I examined the patient with particular care for evidence of a defect at the lower end of the rectus scar. None was appreciable clinically so it was concluded that the lesion was an ordinary inguinal hernia particularly in view of the fact that the patient had had complete relief for many years from the wearing of an ordinary inguinal truss. The frequent occurrence of inguinal hernias following appendectomy had been noted by Illoguet and by Watson, who attributed the occurrence to a weakening of the abdominal wall produced by injury of the nerve supply of the muscles of the internal ring usually the iliohypogastric and sometimes the ilioinguinal nerves.

At operation the hernia proved to be of a variety hitherto undescribed. A true incisional hernia was found which descended from the lower end of the rectus scar behind the rectus and internal oblique muscles to enter the inguinal canal which it traversed to make its exit through the external inguinal ring. While related to those reported by Fisher it differed from them in that it was a true hernia completely enclosed in a peritoneal sac and it made its way to the inguinal canal from a right rectus incision rather than from a McBurney incision as in the cases he reported. While it is likely that such hernias have been encountered by others I was unable to find any such in the literature and hence feel a report is warranted.

CASE REPORT

H. F., a 38 year old man, was seen for the first time on April 16, 1947 at which time he complained of a reducible lump in the right groin. This had been noted first shortly after appendectomy with drainage in 1936. At first it was relatively asymptomatic. Later it caused moderate discomfort for which a truss was prescribed. This helped the hernia effectively reduced and was worn with relief of symptoms for approximately nine years. How

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ever, because of the nuisance involved in wearing a truss and local irritation produced by it, he now desired operative correction. There was a history of bleeding peptic ulcer four years previously, but now he was asymptomatic in this regard and x ray views of the stomach and duodenum taken recently were negative. There was no other significant history.

Physical examination revealed an apprehensive, slightly built adult man with no significant findings apart from the local lesion, where what seemed to be a typical indirect inguinal hernia protruded through the external inguinal ring, descending as far as the upper portion of the scrotum. The hernia was readily reducible and, when reduced, pressure upon the internal inguinal ring maintained reduction through coughing or straining. When pressure upon the internal ring was released, the hernia again promptly descended into the canal and out the external ring. The possibility of an interstitial incisional hernia was considered and the right lower rectus appendectomy scar was examined carefully with this in mind. However, no evidence of deficiency, weakness, or abnormal impulse could be detected along the length of the scar, which seemed solid in its entirety. Accordingly, the lesion was considered to be an ordinary indirect inguinal hernia, anatomically independent of the previous operative site.

The patient was admitted to The Mount Sinai Hospital May 5 1946 (No 548586) and was operated upon May 6. An inguinal incision was made and the external oblique aponeurosis was incised in the direction of its fibers through the external ring. The lower leaf of the aponeurosis of the external oblique was dissected free to expose Poupart's ligament and the upper leaf retracted upward to expose the spermatic cord emerging from beneath the internal oblique muscle. The cremaster fascia was incised and the hernial sac overlying the spermatic cord anterosuperiorly was identified. The sac was opened and a nubbin of omentum which it contained was reduced into the peritoneal cavity. Traction was made upon the sac by a finger placed within it and dissection of the sac from the cord structures was proceeded with. As the dissection was carried proximally, the sac was observed to diverge superomedially from the cord structures in the region of the internal ring. Moreover, it was now recognized that nowhere in its extent had the sac been as closely applied to the cord structures as is ordinarily the case, and a suspicion that an unusual variety of hernia was being encountered, possibly an incisional interstitial hernia which had not been discernible clinically, now began to make itself felt. Further examination in the region of the internal ring revealed that the sac not only actually diverged superomedially from the cord structures at this point, but that it extended as a tubular sac for a considerable distance above this level. Accordingly, the internal oblique and transversus abdominis muscles were divided vertically and the sac was then easily followed in a course leading at first behind the internal oblique muscle and then behind the rectus abdominis to the lower end of the old appendectomy scar where it was seen to emerge from a deficiency in the transversalis fascia. At this point the sac was transected and the excess cut away. The transversalis fascia was closed over the stump. The internal oblique and transversus abdominis muscles were repaired with interrupted sutures. The cord was delivered and the transversalis fascia overlying the direct space and the internal ring were plicated as there seemed to be some loss of normal tautness in these areas. The upper leaf of the external oblique aponeurosis was brought down to the adhering edge of Poupart's ligament and the lower leaf was overlapped across the suture line with subcutaneous transplantation of the cord. The skin was closed with Michel clips.

The postoperative course was entirely uneventful and the patient was discharged with primary healing on the eleventh postoperative day. He was seen for a checkup on Dec 11, 1946 at which time he had no complaints and the wound was solidly healed with no evidence of recurrence or weakness.

COMMENT

Hernias develop interstitially when that is the least resistant path to take. Thus, the ordinary interstitial inguinal hernia is most commonly found in association with an undescended testicle, in which case the preformed processus vaginalis no longer leads to the scrotum and hence eliminates this as the path of least resistance. In Fisher's cases, the pathway between a McBurney in

cision and the inguinal canal is obviously an easy one to traverse as a moment's reflection on the anatomy will show. Actually, a herniation through a defect in the transversalis fascia at the lower angle of a McBurney incision is practically within the inguinal canal since it is situated posterior to the internal oblique muscle which forms the anterior wall of the inguinal canal, and anterior to the transversalis fascia which forms the posterior wall of the canal. To enter the canal itself it needs only to travel a short distance inferiorly in a preformed fascial plane, a pathway which should offer little resistance. Hence, such an occurrence should not be uncommon and it is surprising that there is no record of it prior to Fisher's report.

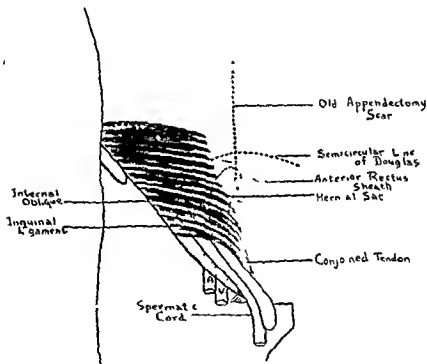


Fig 1—Diagram showing relationship of incisional hernial sac to inguinal canal and spermatic cord.

The pathway in the case reported here does not differ substantially from those in Fisher's cases despite the origin of the hernia from the lower angle of a right rectus incision. In brief the pathogenesis was as follows (Fig 1). A defect in the transversalis fascia doubtless was present at the drainage site at the lower angle of the right rectus incision. This was below the level of the linea semicircularis of Douglas. Arising at this point the peritoneal sac pushed through the defect in the transversalis fascia to lie between it and the rectus abdominis muscle. As the sac developed this plane offered the least resistant

pathway and it pushed its way inferolaterally in a course leading first behind the rectus abdominis muscle and then behind the internal oblique (and transversus abdominis). Once behind the internal oblique its location was the same as in Fisher's cases and entrance into the inguinal canal occurred in identical manner by further downward extension. A crucial point in the pathway the hernia took is the origin of the sac below the level of the line of Douglas. Below this level the rectus muscle lacks a posterior sheath and accordingly no fusion of anterior and posterior sheaths at the lateral border of the rectus exists to prevent the crossing of this border by the hernia. Also since the outer border of the rectus curves inward below the level of the line of Douglas an almost directly downward course of the hernial sac will carry it across the lateral rectus border to a position behind the internal oblique. Therefore a natural fascial pathway is seen to exist along which a hernia developing at the inferior angle of a right lower rectus incision can easily pass to enter the inguinal canal.

The case reported was a true hernia in that it possessed a complete peritoneal sac differing in this respect from Fisher's cases. A common fascial covering enveloped both the sac and the spermatic cord which was presumed to be cremaster fascia acquired from the internal oblique muscle as the sac entered the inguinal canal in the same manner as the spermatic cord acquires its covering of cremaster fascia. However the common covering may merely have been adventitial tissue developing over the nine year period that the hernia existed and the truss was worn.

It is of interest that no sign of origin from the old incision could be detected clinically even though this was specifically sought. The clinical findings were those of an ordinary indirect inguinal hernia. The importance of this surgically is obvious as a cure will not be obtained unless the true nature of the hernia is recognized at the operating table.

SUMMARY

1 A case of a hitherto undescribed variety of hernia is reported. The hernia a postappendectomy incisional interstitial inguinal hernia descended from the lower angle of a right lower rectus incision posterior to the rectus and internal oblique (and transversus abdominis) muscles to enter the inguinal canal which it then traversed.

2 On clinical examination what appeared to be a typical reducible indirect inguinal hernia was found extending through the external inguinal ring into the upper scrotum. The right rectus scar appeared to be solid and the hernia independent of it. Only at operation was the true relationship discovered.

3 The pathogenesis of such a hernia is discussed and the importance of recognizing its true nature is stressed.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

II RENAL FUNCTION STUDIES IN THE WOUNDED

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INTRODUCTION

THE desirability of measuring renal function as accurately as possible in the wounded was clear at the outset of this study. In the majority of cases phenolsulfonphthalein excretory capacity and urine concentration tests where possible (in conjunction with routine urinalyses and blood chemistry determinations) were used as a means of estimating renal function. Mannitol and sodium para amino hippurate for the estimation of glomerular filtration rate effective renal blood flow and maximal tubular excretory capacity did not become available to us until the last weeks of the Italian campaign. The results of the phenolsulfonphthalein urine concentration and the few clearance tests performed will be described.

PHENOLSULFONPHTHALEIN EXCRETORY CAPACITY

Practical considerations prevented estimating phenolsulfonphthalein excretory capacity until after operation. All of the measurements were made postoperatively (or in the few cases which had no surgery after the patients had been transferred from the shock ward) and usually many hours after adequate resuscitation had been effected. Two main groups are included: (1) that in which the test was done within seventy-two hours after wounding and (2) that in which it was repeated after the third day if initial excretory capacity was impaired in order to follow the rate of recovery. Included in the latter group are three patients in whom initial phenolsulfonphthalein tests were done later than the third day after wounding but in whom the quantity of dye excreted was low.

Technique of Test—The following technique of performing this test was commonly employed. Six milligrams of phenolsulfonphthalein were injected intravenously and urine collections made 15, 30, 60 and 120 minutes later.

Wounded
(Continued)

It was necessary to use an indwelling catheter in practically every case to insure accurate collection. Oral intake of fluid was restricted in most patients at the time the test was performed therefore in order to promote urine flow a liter of 5 per cent glucose in normal saline solution or 10 per cent glucose in distilled water was frequently started intravenously about one half hour before injection of the dye.

Excretory Capacity in the First Three Days After Wounding—The average results of the test and other pertinent data in 57 cases* during this period are shown in Table I and Fig 1.

The most striking feature is the difference between the percentages of dye excreted by the 20 patients with no shock and the percentages of dye excreted by the 37 patients with slight moderate and severe shock. Average excretion during all periods was normal in the no shock group (see discussion to follow on relation to type and duration of anesthesia in this group). During the first half hour excretion was low in all patients with initial shock and was lower with increasing severity of shock. Although standard errors of the mean are rather large and although there are no significant differences among the three groups with slight moderate or severe shock the qualitative variations are evident. After the first half hour average dye excretion became normal in all patients except the 14 with severe initial shock. In these 14 patients the average excretion was significantly less than normal even after two hours.

The total amount and rapidity of dye excretion are well correlated with average nonprotein nitrogen values determined on the same days the dye was given as shown by the higher average nonprotein nitrogen values in each group according to severity of shock (see Table I). Likewise the number of cases with high azotemia oliguria or anuria rises with increasing severity of shock†.

Incidence of initial hypotension (systolic blood pressure 80 mm. of mercury or less) increases with severity of shock. 25 or 26 patients with severe or moderate shock had low blood pressure during the period of shock.

Effect of Anesthesia—One might argue that the diminished ability to excrete phenolsulfonphthalein in these cases was largely or partially due to the effect of anesthesia especially ether. Our data indicate that this is not true. In the 20 patients with no shock and in whom phenolsulfonphthalein excretion was normal (Table I and Fig 1) the anesthetic agents employed were as follows: ether alone 3 cases, pentothal alone 1 case, pentothal induction followed by ether 16 cases. The average length of anesthesia in these 20 was 1.69 ± 0.21 hours; the phenolsulfonphthalein test was started on the average 8.39 ± 1.25 hours after anesthesia was ended. If ether per se had any marked effect

*Twenty-one of these are not included in our total series of 186 patients. They were collected merely to enlarge the series of phenolsulfonphthalein tests without attempting to do complete studies. Seventeen of the 21 had no shock, 1 slight shock and 2 moderate shock.

†The high azotemia group includes all patients whose nonprotein nitrogen rose to 45 mg. per cent or higher at some time during the post-traumatic period. The oliguria group includes patients with a twenty-four hour urine output of 100 to 400 cc. at least once during the post-traumatic period. The anuria group includes patients with a urine output of less than 100 cc. daily.

TABLE I

DEGREE OF INITIAL SHOCK	TOTAL NUMBER OF CASES*	THROMBOLYTIC-PHYSEPTIN IN PERCENTAGE INCREMENTS				HOURS FROM WOUNDING TO TEST (AVERAGE)	M.F.N. ON DAY OF TEST (AV. NO. %)	"HIGH AZOTEMIA" (NUMBER OF CASES)	OLIGURIA OR ANURIA (NUMBER OF CASES)	INITIAL HYOTEN- SION† (NUMBER OF CASES)
		15 MIN	30 MIN	40 MIN	120 MIN					
None	26	11.0 +2.47	50.5 +2.57	11.9 +2.86	73.3 +2.82	39.03 +2.25 (Max 43)	28 +1.2	0	1	0
Slight	11	16.80 +7.47	34.55 +4.06	51.45 +3.68	61.0 +5.9	30.04 +2.54 (Max 46)	31.38 +2.04	0	3	2
Moderate	12	12.73 +2.77	71.25 +3.56	49.09 +7.12	60.08 +7.73	31.25 +1.22 (Max 40)	47.08 +4.44	3	4	11
Severe	14†	0.00 +3.45	25.22 +6.42	16.19 +9.66	47.62 +9.0	37.4 +3.05 (Max 60)	47.8 +4.2	7	8	14

Standard errors of the mean are shown

*Includes one crush patient who was not operated on; all other tests were done postoperatively

†Initial pressure 80 mm Hg or less

upon dye excretion, it should be evident in this group in which shock and hypotension were absent. Further evidence that anesthesia did not affect the ability of the kidneys to excrete phenolsulfonphthalein in this series is that the average time between wounding (and hence in most cases between anesthesia) and determination of excretory capacity was considerably greater in those cases which showed greatest diminution of excretory capacity (Table I). Ether was used in all 37 patients with diminished excretion and coincident varying degrees of shock, except one patient with a crushing injury who had no anesthesia.

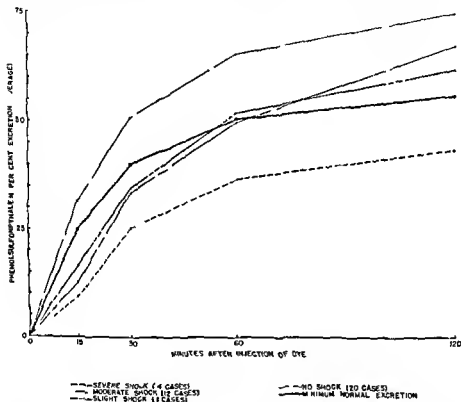


FIG. 1—Average phenolsulfonphthalein excretory capacity in 37 wounded patients classified according to degree of initial shock. Increments of percentage of phenolsulfonphthalein excreted are represented. Observations are discussed in the text. (Minimum normal excretion statistics from Stitt, Clough, and Clough.)

Rate of Recovery of Phenolsulfonphthalein Excretory Capacity—For those interested in details Table II is included showing phenolsulfonphthalein excretion and other pertinent data on 15 patients in whom the test was repeated one or more times.

Table II shows that of 15 patients in whom the test was done on the fourth or fifth postoperative day 7 had normal excretion. All of these 7 had abnormal excretion during the first three days after wounding: 2 had moderate initial shock, 3 slight shock, and 2 no shock. Of the 8 patients in whom dye excretion was low on the fourth or fifth postoperative days, 3 had undergone the test

TABLE II. RATE OF RECOVERY OF PHENOL-SULFONPHENYLALANINE EXCRETORY CAPACITY FOLLOWING WOUNDING

CARE NUMBER	TIME, WOUNDING TO TEST	1:1 PHENOL-SULFONPHENYLALANINE FACILITY (PERCENTAGE)				PERCENT DAY OF TEST (NO. %)	DEGREE OF INITIAL SHOCK	INITIAL HYPO TENSION	"HIGH AZO TEMIA,"	URINE OUTPUT	REMARKS
		15 MIN	30 MIN	60 MIN	120 MIN						
81	3 hr	03	20	34	50	77	Severe	++	Yes	Oliguria	Uneventful recovery
90	3 days	10	190	330	530	50					
	24 hr	07	13	20	35	58	Severe	++	Yes	Oliguria	Recovery diarrhea
	9 days	10	20	30	50	108					
	12 days	210	180	250	340	46					
125	4 days	30	310	430	520	73					
104	34 days	30	60	100	150	108	Severe	+	Yes	Oliguria	Recovery of azotemia
	7 days	280	110	470	270	15	Moderate	+	Yes	Oliguria	Recovery diarrhea
	11 days	50	90	140	300	29					
107	23 hr	00	500	690	780	59					
63	5 days	00	150	-10	280	42	Moderate	++	Yes	Normal	Died 6th day, alkalosis uremia contributory
	5 hr	00	10	30	170	73					
1	4 days	00	180	780	630	43	Moderate	++	No	Oliguria	Uneventful recovery
	8 days	20	40	310	390	31					
	17 hr	00	440	620	720	25					
20	4 days	430	500	690	760	54	Moderate	+	No	Oliguria	Uneventful recovery
	4 days	00	110	400	590	36					
	5 days	200	410	610	750	49	Moderate	+	Yes	Oliguria	Stormy course, probable blood stream infection
53	31 hr	90	110	200	560	37	Moderate	+	No	Oliguria	Uneventful recovery
15	4 days	10	480	630	770	27					
	24 hr	30	420	550	700	30	Slight	+	No	Oliguria	Uneventful recovery
83	3 hr	470	530	770	770	31					
111	4 days	65	230	780	840	26	Slight	0	No	Normal	Uneventful recovery
	11 hr	50	190	780	890	24					
129	5 days	20	310	650	740	30	Slight	0	No	Normal	Uneventful recovery
	20 hr	410	430	710	740	48					
106	7 days	160	190	390	400	31	Slight	0	No	Normal	Uneventful recovery
	10 days	220	230	470	450	39					
102	10 days	200	470	670	730	24	None	0	No	Normal	Uneventful recovery
	15 hr	400	570	770	810	24					
43	5 days	180	280	490	730	43	None	0	No	Normal	Uneventful recovery
	5 days	420	610	760	840	43					

for the first time during this period and 5 are known to have had diminished excretion during the first three days. Of these 8 patients the degree of initial shock was slight in one, moderate in 4 and severe in 3. Three cases conformed with the syndrome of recovery diuresis.

The test was repeated between the eighth and fourteenth days in 4 patients. One had normal dye excretion by the eleventh day. Another had slightly diminished excretion during only the first fifteen minutes on the eighth day. Two who had recovery diuresis still had abnormal excretion on the twelfth and fourteenth postoperative days respectively.

With the exception of one patient who died with alkalosis and renal failure (Case 107, Table II) all patients in whom initial test results were low showed improved dye excretion as tests were repeated. Improvement was reflected chiefly in ability to excrete increased amounts of dye during the first thirty minutes although total amount excreted increased also with passage of time.

The time required for phenolsulfonphthalein excretory capacity to return to normal is well correlated with urine output, nonprotein nitrogen retention and degree of initial shock and hypotension (see Table II). In general, those with normal urine output or only slight suppression, minimal nitrogen retention and slight shock recovered most rapidly.

RENAL CLEARANCE STUDIES

The predominance of histologic changes in the lower nephron and the paucity of glomerular damage seen in the kidneys of patients who died of this syndrome immediately raised the question of how much functional impairment corresponds with anatomic alterations.¹ One obvious approach to solution of this problem would be in utilization of clearance methods of measuring renal function. This was done in 11 patients—a small series but the largest obtainable after the materials necessary for performance of the tests became available.

Methods.—Mannitol was used for measurement of glomerular filtration rate (C_{M}); sodium para amino hippurate for effective renal plasma flow (C_{EAP}) and maximal tubular excretory capacity (Tm_{PAH}). Methods of analysis are described in a separate report.¹ Quantities, given and rates of administration were essentially those suggested by Goldring and Chasis.² Indwelling multiple cycled catheters were routinely employed. The bladder was washed with 10 to 30 c.c. of physiologic saline solution at the end of each collection period followed by 10 to 20 c.c. of air to insure complete emptying of the bladder. Protocols are included with the individual case histories and contain complete details.¹

Types of Cases (Table III).—Five patients were studied within the first thirty-one hours after wounding but after resuscitation had been effected and operation completed. One of these had no initial shock, 1 slight, 2 moderate, and 1 severe. None had a nonprotein nitrogen of 65 mg. per cent or over that is, high azotemia while we observed them. Urine output was normal throughout in 4. One patient was listed as having had oliguria in our original sense for one day (Case 142) but the oliguria was not severe and can be disregarded since on the preceding and succeeding days urine output was satisfactory.

TABLE III SUMMARY OF RENAL CLEARANCE STUDIES

CASE NUMBER	TIME FLOW— (cc PER MIN)	PLUTATION RATE (cc PER MIN)	EXCRETIVE PLASMA FLOW (cc PER MIN)	EXCRETIVE BLOOD FLOW (cc PER MIN)	TEMPERATURE (°C PER MIN)	FILTRATION FRACTION	C _{PAH} /TEMPERATURE	C _{IN} /TEMPERATURE	TIME OF RENAL CLEARANCE AFTER WOLVING	DEGREE OF INITIAL SHOCK	"HIGH AZOTEMIA"	% OF DAT OF TEST	CRINE OUTPUT	PLATE OUTPUT OF DAY OF TEST (cc)	BLOOD PRESSURE OF DAY OF TEST	RECOVERY
131	3.0 (3)	0.2 (2)	5.5 (1)	1.71 (1)	84 (2)	0.15 (1)	5.8 (1)	0.81 (1)	1 hr	None	No	43	Normal	1635	114	Recovery
141	4.8 (4)	1.7 (4)	10.3 (1)	10.3 (1)	56 (2)	0.11 (2)	12.3 (1)	2.50 (2)	19 hr	Slight	No	41	Normal	2120	120	Recovery
142	4.8 (4)	1.5 (4)	7.5 (2)	11.5 (1)	93 (2)	1.25 (2)	8.1 (2)	1.75 (2)	14 hr	Moderate	No	37	Oliguria	1603	180	Recovery
143	7.8 (3)	1.0 (4)	5.2 (2)	8.16 (1)	73 (2)	0.20 (2)	9.0 (2)	1.00 (2)	31 hr	Moderate	No	40	Normal	1757	170	Recovery
144	5.2 (4)	1.1 (4)	14.1 (2)	5.56 (2)	97 (2)	0.14 (1)	13 (2)	0.80 (2)	20 hr	Severe	No	10*	Normal	3762	70	Recovery
145	7.4 (4)	8.3 (4)	50.8 (2)	10.7 (1)	168 (2)	0.1 (2)	5.1 (1)	0.81 (2)	3 days 14 hr	Moderate	Yes	57	Normal	1986	74	Recovery
146	2.34 (4)	2.0 (4)	9.6 (2)	7.91 (2)	7 (2)	0.21 (1)	13.4 (2)	2.2 (2)	17 days	Severe	Yes	108	Unknown, probably oliguria	12704	150	Uremia coincident at least 5 days later Recovery begins
147	2.34 (4)	2.0 (4)	9.6 (2)	7.91 (2)	7 (2)	0.21 (1)	13.4 (2)	2.2 (2)	17 days	Severe	Yes	108	Unknown, probably oliguria	12704	150	Recovery

	4.0 (3)	5.6 (3)	13 days	Severe	Yes	125	Unknown, probably oliguria	-380	140 110	Recovery diuresis
133	4.0 (3)	5.6 (3)								
137	3.42 (3)	5.8 (3)	28 days	Severe	Yes	36	Unknown, probably oliguria	Over 1000	122 96	Recovery diuresis
137	4.33 (2)	15.71 (4)	47 days	Severe	Yes	24	Unknown, probably oliguria	Over 1000	120 70	Recovery diuresis
137	9.14	10.71 (2)	40 days	Severe	Yes	20	Unknown, probably oliguria	Over 1000	120 70	Recovery diuresis
147	4.1 (4)	6.4 (4)	7 days 18 hr	Severe	Yes	99	Normal	1558	110 60	Uremia coincident at death, 16 hr. later
150	5.72 (4)	8.0 (4)	30 days	Severe	Yes	26	Oliguria	1500 + 500	130 91	Recovery diuresis
150	4.42 (4)	15 (4)	14 days	Moderate	Yes	123	Anuria	3350	170 100	Recovery diuresis
150	4.74 (4)	10.0 (4)	26 days	Moderate	Yes	24	Anuria	3000±	130 70	Recovery diuresis
178	7.0 (4)	3 (4)	10 days	None	Yes	217	Unknown, probably oliguria	1500±	140 68	Recovery diuresis
178	5.54 (4)	6.4 (4)	26 days	None	Yes	44	Unknown, probably oliguria	4500±	128 70	Recovery diuresis

Mean 131 ± 1.7 1204 ± 76 19 ± 9.2 172

nor 215 135.9 255.9 0.0244

Numbers in parentheses represent number of periods averaged. Values in Columns 3 through 8 corrected to 1.77 square meters of body surface.

Normals and standard deviations from Goldring and Chasis* and Smith*.

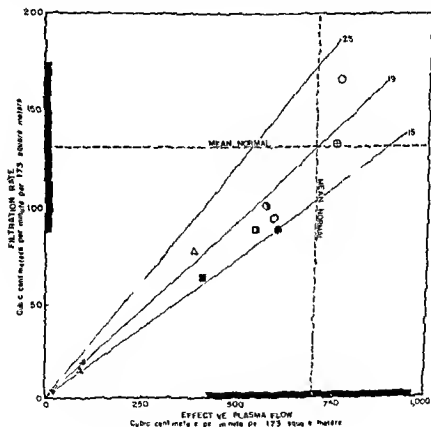
*One day later.

†Plasma mannitol levels below 1.0 mg per cubic centimeter so observed filtration rate possibly too high.

‡Only 2 of 5 periods averaged. Last 3 during sucrose Tm determination fell rapidly giving average of 89 if they are included.

§Calculated from PAH done two days previously.

The remaining 6 patients were first studied between three and thirty days after wounding. All of them had "high azotemia" at some time during their course. One had no shock, 2 moderate, and 3, severe. In 3 patients clearances were first measured while renal failure was severe, and repeated after recovery diuresis had taken place. A fourth had severe renal failure, but



- No shock, no azotemia, 29 hours after wounding
- Slight shock, no azotemia, 9 hours after wounding
- △ Moderate shock, no azotemia, 4 hours after wounding
- ◇ Moderate shock, no azotemia, 3 hours after wounding
- ▲ Severe shock, no azotemia, 20 hours after wounding
- Moderate shock, azotemia, 35 days after wounding
- Severe shock, azotemia, 775 days after wounding
- ◆ Severe shock, azotemia, recovery diuresis, 30 days after wounding
- ▲ Severe shock, azotemia, recovery diuresis, 11 days after wounding
- ▲ Moderate shock, azotemia, recovery diuresis, 4 days after wounding
- ▼ No shock, azotemia, recovery diuresis, 0 days after wounding

clearances were not done until thirty days after wounding, by which time he had a recovery diuresis and plasma nonprotein nitrogen was normal. The remaining 2 died sixteen hours and five days respectively, after clearance studies were done, in both cases uremia was coincident at death but not a primary or contributory cause of death.

Further pertinent details will be found in Table III and the individual case histories.¹

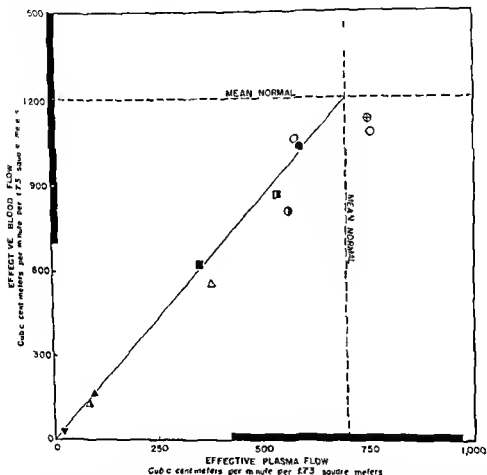


Fig. 3—Relationship between effective plasma flow and effective blood flow. Symbols are explained in Fig. 2. Note influence of hemorrhage in producing a somewhat greater reduction in total effective blood flow than effective plasma flow. Mean normals from Smith.⁴

Results—All 11 cases are included in Table III and in Figs. 2 through 5, these figures are constructed from average values listed in Table III. In the 3 with the lowest values (Cases 133, 138 and 150) in whom tests were repeated only the initial observations are shown in Figs. 2 through 5. These same initial observations and those noted when the tests were repeated are represented in Figs. 6 through 8.

1 *Filtration Rate and Effective Plasma Flow* (Table I) and Fig 2) The values for the filtration rate and plasma flow were significantly below normal in one patient twenty hours after wounding (Case 139), he was the only one of the 5 studied during the early postoperative period who had severe initial shock. In 2 other patients glomerular filtration rate and plasma flow were in low normal ranges

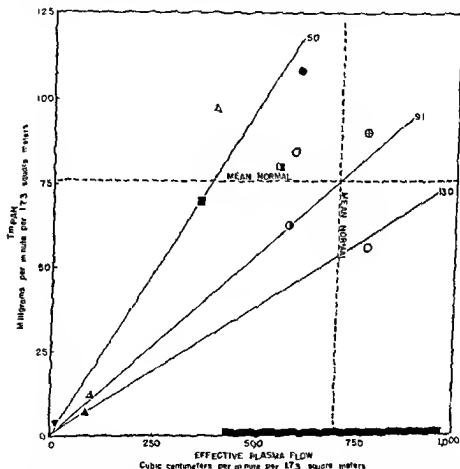


Fig 4.—Relationship between effective plasma flow and maximal tubular excretory capacity. Mean normal of plasma flow is the same as in Fig 2. Normal for Tm_{PAH} from Goldring and Chasis (p 56) for which there was not a sufficiently large series for statistical treatment—hence no standard deviations are shown. Diagonal lines represent $\frac{Cr_{PAH}}{Tm_{PAH}}$. Variation is wide but noteworthy perhaps is the fact that all but two cases had ratios less than normal.

Marked diminutions of both components in the 3 patients with severe renal failure are evident (Cases 133, 138 and 139). There are lesser degrees of impairment in the 2 in whom renal failure was only coincident in subsequent death (Cases 143, 147), and in the patient who had fairly well recovered from renal failure (Case 125).

The tendency of glomerular filtration rate and effective plasma flow to diminish proportionately are demonstrated in most cases by the relatively normal filtration fractions ($\frac{C_M}{C_{PAH}}$). Each of the three patients with very low filtration rates and plasma flow had moderate hypertension at the time the tests were performed. In none are the high filtration fractions characteristic in essential hypertension present.

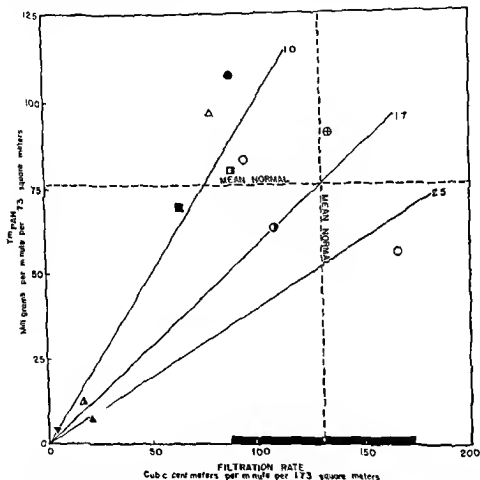


FIG. 5—Relationship between filtration rate and maximal tubular excretory capacity normals derived from sources mentioned in Figs. 2 and 4. There is a tendency for ratio of $\frac{C_M}{C_{PAH}}$ to be above normal.

2 *Effective Renal Blood Flow* (Table III, Fig. 3). Here the influence of low hematocrit is shown. Total effective blood flow is proportionately reduced more than effective plasma flow in most cases.

3 *Maximal Tubular Excretory Capacity* (Table III, Fig. 4). Variation is wide in measuring maximal tubular excretory capacity, but it was significantly low only in the 3 patients with marked renal failure. It is of interest that the

one patient with severe initial shock who was studied twenty hours after wounding had low filtration rate and renal blood flow but normal T_m (Case 139). Relating plasma flow to maximal excretory capacity ($\frac{C_{PAH}}{T_{mPAH}}$), diagonal line in Fig 4, gives an expression of the virtual quantity of plasma cleared per unit of functionally active tubular tissue. Ratios below normal should in

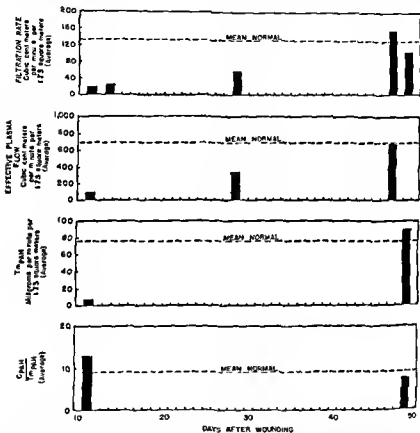


Fig 6—Patient with severe renal failure and subsequent recovery diuretics (Case 123). Mean normals are those used in Figs 2 through 5 and average values are those given in Table III. The $\frac{C_{PAH}}{T_{mPAH}}$ ratio represented on the forty-ninth day was calculated by using C_{PAH} measured two days previously. Not (1) relatively proportionate reduction in glomerular filtration rate, effective plasma flow and maximal tubular excretory capacity and (2) similar recovery rates for all three components.

dicate relative renal ischemia. It may be significant that this ratio was normal or below normal in 9 cases, and that it was lowest in the patient tested shortly after he had recovered from severe shock (Case 139).

Relating filtration rate to maximal tubular excretory capacity ($\frac{C_{SC}}{T_{mIAH}}$), diagonal line in Fig 5, gives an expression of glomerular function per unit of

functioning tubular tissue. Ratios below normal should indicate greater relative impairment of glomerular function than tubular and high ratios the reverse. Nine of the 11 have either a normal or a low ratio—a fact difficult to explain in view of the anatomic lesion in this type of case.

4 *Rate of Recovery* (Table III Figs 6, 7 and 8). Three patients who had severe renal failure but recovered are represented. Initial observations were made during periods of maximum failure; subsequent ones after recovery had largely taken place. In general, on the basis of clearance measurements

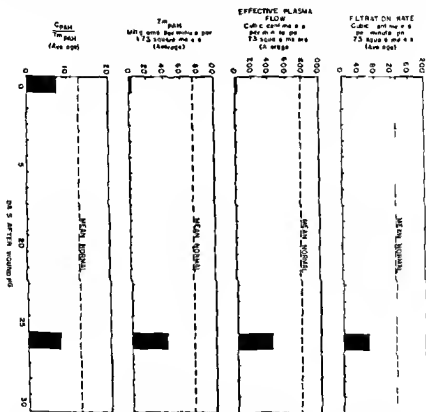


Fig. 7—Patient with severe renal failure and subsequent recovery. Illustrations (Case 1-0). Sources are the same as mentioned in Fig. 6.

all portions of the nephron were about equally affected; recovery likewise occurred at about an even rate in all portions. Restitution of function was apparently complete forty-nine days after wounding in 1 patient (Fig. 6); partially so in the other 2 patients twenty-six days after wounding (Figs. 7 and 8).

URINE CONCENTRATION TESTS

Although the value of the urine concentration test was self-evident, practical difficulties prevented our using it as a measure of renal function in many cases. Fluid restriction during the first few postoperative days was almost

one patient with severe initial shock who was studied twenty hours after wound ing had low filtration rate and renal blood flow but normal T_m (Case 139)

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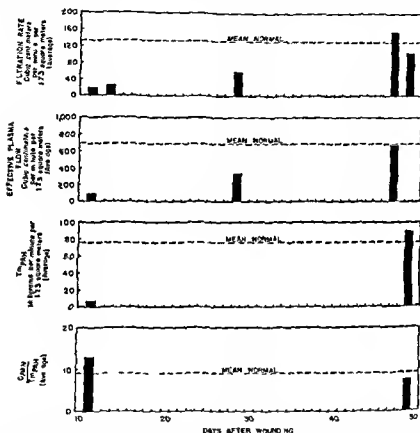


Fig 6.—Patient with severe renal failure and subsequent recovery diuresis (Case 123). Mean Normals are those used in Figs 2 through 5 and average values are those given in Table III. The $\frac{C_{PAH}}{T_{mPAH}}$ ratio represented on the forty-ninth day was calculated by using C_{PAH} measured two days previously. *Note:* (1) relatively proportionate reduction in glomerular filtration rate, effective plasma flow and maximal tubular excretory capacity and (2) similar recovery rates for all three components.

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TABLE IV

SPECIFIC GRAVITY OF URINE	DAYS FROM WOUNDING TO FIRST TEST	DEGREE OF INITIAL SHOCK (NO OF CASES)				INITIAL HYPOTENSION (NO OF CASES)	OLIGURIA OR ANURIA (NO OF CASES)	'HIGH AZOTEMIA' (NO OF CASES)	TOTAL NUMBER CASES
		NONP	SLIGHT	MOD	SEVERE				
Over 1.020	1 to 7	3	6	5	3	8	6	2	17
1.018 to 1.024	2 to 8	0	1	8	0	5	5	1	9
Under 1.018	1 to 17	1	1	1	3	4	5*	5	6

*Actual output unknown in two cases but good presumptive evidence of oliguria present

Of the 17 patients in whom there was no impairment of concentrating ability during the first week after wounding 8 had initial moderate or severe shock and initial hypotension. Two of these 17 subsequently had high azotemia. Of the 9 patients with slightly decreased ability to reabsorb water from the kidney tubules (specific gravity 1.018 to 1.024) 8 had moderate initial shock 5 initial hypotension 5 oliguria or anuria and one high azotemia. In the group of 6 cases with marked impairment of concentrating ability 4 had moderate or severe shock and 4 had hypotension. Five of these 6 had marked and prolonged azotemia and have been discussed previously in this paper and elsewhere.^{1, 2}

The test was done more than once in 8 patients. Of 2 in whom concentration was 1.018 at the time of the first test each concentrated to 1.020 two and seven days later respectively. One whose specific gravity at first was 1.017 concentrated to 1.022 three days later. Of the 3 cases just mentioned one also had high azotemia and oliguria and 2 had normal urine output and nonprotein nitrogen under 65 mg per cent. The remaining 5 had recovery diuresis and after periods of fourteen to forty days were still unable to make a concentrated urine.

Although this series is very small there is a suggestion that the concentrating function of the kidneys follows somewhat the same pattern as the ability to excrete phenolsulfonphthalein, mannitol and sodium para amino hippurate. Ability to concentrate urine may diminish following shock and improve over a period of three to seven days unless renal failure is severe (recovery diuresis) in which case maximal tubular reabsorption of water remains diminished for many days or weeks. In two cases specific gravity was fixed even after clearance of mannitol and sodium para amino hippurate had returned to normal (Cases 125 and 133').

DISCUSSION

It has been demonstrated by Lawson Bradley and Courmand⁴ that during the state of shock glomerular filtration rate and effective plasma flow are reduced. These workers have further advanced evidence that reduction in renal blood flow is mediated by active vasoconstriction of the renal blood vessels as well as by reduction of arterial pressure.

None of our studies were carried out during the state of shock. Those performed in the first few days after trauma suggest that the reduction in

always inadvisable for the patients' welfare Pituitrin was therefore employed, using the accepted method of administering 0.5 cc of posterior pituitary extract (10 units) subcutaneously and collecting urine specimens one and two hours afterward Many of the patients in whom we should like to have known concentrating ability were receiving considerable amounts of sodium chloride intravenously daily Since the antidiuretic hormone is less effective after salt induced diuresis the number of patients in whom the pituitrin test would have

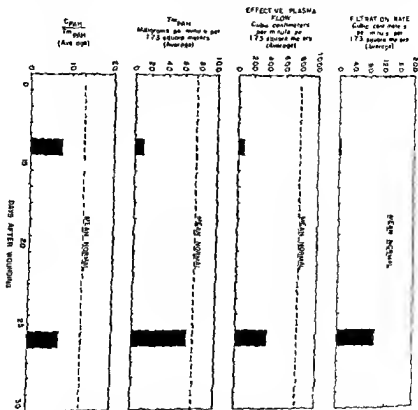


Fig 8.—Patient with severe renal failure and subsequent recovery diuresis (Case 134). Sources are the same as mentioned in Fig 5.

been complicated by recent administration of normal saline solution was large, but in most instances we did not feel justified in requesting that the saline solution be withheld. A compromise regimen was established in which all parenteral fluids were withheld for a period of seven to eight hours before the pituitrin was administered, where such restriction would clearly not be harmful in any way to the patient.

Data on the 32 patients in whom concentrating ability of the kidneys was tested in this manner during the postoperative days indicated are shown in Table IV.

sufficiency. The results suggest that all portions of the nephron suffer functional impairment.

5. Ability to produce a concentrated urine may diminish following shock and rapidly improve over a period of three to seven days, unless renal failure is severe, in which case maximal tubular reabsorption of water is impaired for many days. In two cases urine specific gravity remained fixed and low even after glomerular filtration rate, effective renal plasma flow, and maximal tubular excretory capacity had returned to normal.

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kidney function may persist for some days after shock is relieved even though the usually accepted signs of renal failure (suppression of urine output nitrogen retention) may be meager. These patients probably rapidly regain normal kidney function.

If the initial insult, whatever it is, is greater, the resulting renal insufficiency is much more severe and prolonged, and in a significant proportion of instances results in death in uremia. A few patients do recover, however, with gradually increasing function over a period of days to weeks as indicated by rate of recovery of ability to excrete phenolsulfonphthalein, by improved glomerular filtration, by increased effective plasma flow, maximal tubular excretory capacity, and concentrating capacity of the urine.

Although the histologic picture in fatal cases might suggest a selective functional impairment of the lower nephron¹ our studies indicate that all functional components of the kidneys are about equally impaired. Glomerular filtration rate and effective plasma flow were reduced in essentially proportionate degrees in most of the patients we studied. That there may have been some relative ischemia in these cases is suggested by the fact that in the few cases

where clearances were done the ratio of $\frac{C_{\text{IAH}}}{T_{\text{MFAH}}}$ showed a tendency to be low.

One bit of evidence in favor of greater relative insult in the lower nephron should be cited from the two cases in which ability to concentrate urine was still much impaired after clearances had returned to normal. Mannitol serves as a measure of glomerular filtration, sodium para amino hippurate is believed to be excreted in the proximal tubules. Urine concentration takes place further down the nephron in the loop of Henle. Is this lag in recovery of concentrating capacity a manifestation of greater relative damage to the lower nephron?

SUMMARY

1 The results of measurements of phenolsulfonphthalein excretory capacity, glomerular filtration rate, effective renal blood flow, maximal tubular excretory capacity, and urine concentration tests following wounding and subsequent resuscitation if shock was present have been presented.

2 Phenolsulfonphthalein excretory capacity determined within seventy-two hours after wounding and after resuscitation had been effected and surgery completed was significantly diminished in patients with initial shock and was normal in those without initial shock. Where this measurement was repeated excretory capacity rapidly returned toward normal during the first two weeks after wounding in those patients with evidence of minimal renal failure and more slowly in those with signs of more severe kidney damage.

3 One of 5 patients showed significantly low glomerular filtration rate and effective plasma flow but normal maximal tubular excretory capacity thirty hours after wounding and severe initial shock. Measurements of the same functions were normal in the other 4 patients studied in the early period after wounding; none of whom had appreciable shock.

4 Six patients who had a nonprotein nitrogen of 6+ mg. per cent or higher after wounding were studied during various phases of their renal in-

The amount of skin removed should be extensive. Three fingerbreadths from the edge of the tumor on all sides should be a minimum.

In women in the premenopausal period, it is important to give additional irradiation to the ovaries. Radical mastectomy should not be performed if one of the following is present: (1) distant metastases, (2) secondary or daughter growths in the skin, (3) fixation of the growth to the chest wall, (4) fixation of the nodes in the axilla, (5) swelling and edema of the arm.

Simple mastectomy, combined with pre- and postoperative irradiation is sufficient in the older age group. Extreme radicalness should be reserved for the younger patient.

Warren H. Cole, LeRoy Walter, and John Reynolds, Chicago. **Surgical Treatment of Peptic Ulcer**—Thirty cases were analyzed in which vagotomy was performed for peptic ulcer with no operative mortality. In all cases, there was a marked diminution in gastric acidity and relief of pain. The following are the indications for vagotomy: (1) intractable symptoms, (2) pyloric obstruction unrelieved by medical measures (gastroenterostomy or gastrectomy should be done along with the vagotomy), (3) gastropyloric ulceration, (4) gastric ulcers in which a high acidity is present and in which there is no suggestion of malignancy.

The insulin test will determine the degree of completeness of the vagus nerve section. The complications of vagotomy are not severe. Gastric retention can be eliminated by adequate postoperative decompression. The Abbott-Rawson tube was used postoperatively in this series. Cole and his associates prefer the abdominal approach for vagotomy, in order to inspect the ulcer and perform gastroenterostomy if necessary.

Virgil S. Counseller, Rochester, Minn. **The Etiology and Treatment of Vesicovaginal Fistula**—Vesicovaginal fistulas are of three types: (1) postoperative, (2) post-irradiation or radium therapy, (3) postpartal.

The most common type is the postoperative fistula. The operative procedures most often followed by fistulas are total abdominal hysterectomy, vaginal hysterectomy, and vaginal plastic. Total hysterectomy is not as widely indicated as some are inclined to recommend.

The bladder is injured in one of two ways: (1) It may be actually cut, (2) a suture may be passed through the wall of the bladder into the lumen. When the latter of these two accidents occurs the fistula does not appear for seven to ten days.

Counseller advised strongly against the use of right angle clamps on the upper part of the vagina, because of the danger of including parts of the bladder in the clamp. The risk of infection is slight when the vagina is opened. Direct vision with good hemostasis enables the operator to be certain of not burning the bladder.

Adequate urologic examination is important. The position and type of fistula can be determined. If the ureter is involved and there is kidney infection, nephrectomy is indicated. If the ureter is involved and there is no evidence of kidney infection it may be possible to reimplant the ureter.

In the treatment of a postirradiation fistula, surgical repair should be postponed for at least three years. It is often necessary in such cases to transplant the ureter to the colon.

A motion picture was shown demonstrating the operative technique for the repair of a vesicovaginal fistula. Vaginal examination should not be performed for at least twenty-one days following operation.

Leonard W. Edwards, Nashville. **Results in Biliary Tract Surgery**—Two hundred cases, in which biliary surgery was performed, were analyzed. There were 199 cholecystectomies and one cholecystostomy. Twenty-eight of these cases were acute cholecystitis and of the 27 had stones. Ninety per cent of all the patients showed the presence of stones. The end results are not good in cases in which there is only questionable pathology in the biliary tract.

Review of Recent Meetings

THE FIFTEENTH ANNUAL SESSION OF THE SOUTHEASTERN SURGICAL CONGRESS POSTGRADUATE ASSEMBLY

LOUISVILLE, KY, MARCH 10 TO 12, 1947

MARSHALL L. MICHEL, JR., M.D., NEW ORLEANS, LA

The fifteenth annual session of the Southeastern Surgical Congress Postgraduate Assembly was held at the Brown Hotel Louisville, Ky., on March 10, 11, and 12, 1947.

E. L. Henderson presided and B. T. Beasley served as secretary. J. B. Lukins was general chairman of the committee on arrangements.

R. S. Dinwiddie, Cleveland: Surgical Aspects of Thrombocytopenic Purpura.—Other platelet depressing conditions must be ruled out. The bone marrow is usually normal in thrombocytopenic purpura. Any slight abnormality is merely a reflection of blood loss. The megakaryocytes fail to demonstrate qualitative or quantitative alteration.

If the spleen is enlarged, one is probably not dealing with essential thrombocytopenic purpura. The typical microscopic picture shows a slight generalized hyperplasia of the pulp and lymphoid tissue with little or no fibrosis and no unusual pigmentation or abnormal cells.

The anesthetic of choice for splenectomy is nitrous oxide and ether. Dinwiddie recommended a left oblique subcostal incision. The spleen is delivered medially and forward and a pack placed in the posterior fossa. The gastro-splenic omentum is divided and the vasal branches are ligated. The hepatocolic ligament can then be plainly visualized and ligated. If adhesions to the colon are present, these should be clamped and ligated.

The vessels of the splenic pedicle are dissected and ligated separately. En masse ligation is permissible but not desirable. The spleen can then be removed in toto. The splenic pedicle should be again carefully inspected. The abdomen is closed in layers with interrupted sutures of cotton.

Dinwiddie reported a series of twenty-eight cases of splenectomy for thrombocytopenic purpura. The average age was 26 years and 8 months. There were three deaths, a mortality of 10.7 per cent. Twenty-two patients (78.6 per cent) were cured or markedly improved. Of six patients in whom splenectomy was advised but not performed, four died.

Postoperative evaluation of the patient depends entirely on whether or not bleeding stops and how the patient feels. It is no longer believed that a marked platelet response indicates a good prognosis. In many cases in which good results were obtained the platelets increased only slightly.

The most common cause of death is cerebral hemorrhage. Intractable headache is often a premonitory symptom of this serious complication.

William P. Nicolson, Jr., Atlanta: Carcinoma of the Breast—Its Prevention and Treatment.—There are four conditions which contribute to the development of cancer of the breast, (a) improper or no support, (b) irritation, (c) mastitis, (d) stagnation.

The importance of a properly fitting brassiere as correct support of the breast was emphasized. Mastitis is often a premalignant condition. The use of the breast pump to prevent intraductal stagnation is an important phase in the proper care of the female breast.

The treatment of cancer of the breast is determined by four factors: (1) extent of the disease, (2) nature of the tumor, (3) age of the patient, (4) physical condition of the patient. The treatment should be individualized to fit each particular case. As a rule, however, it should be radical and should combine surgery with pre and postoperative irradiation.

The amount of skin removed should be extensive. Three finger breadths from the edge of the tumor on all sides should be a minimum.

In women in the premenopausal period, it is important to give additional irradiation to the ovaries. Radical mastectomy should not be performed if one of the following is present: (1) distant metastases; (2) secondary or daughter growths in the skin; (3) fixation of the growth to the chest wall; (4) fixation of the nodes in the axilla; (5) swelling and edema of the arms.

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The vascular changes in cholecystitis are important, especially in the aged. Bacterial infection plays a secondary role. Therefore, cholecystectomy is indicated early in the disease, before infection occurs.

There were thirteen perforations, nine of which occurred in the gall bladders with acute conditions, representing 32 per cent of the acute cases. The signs of impending perforation are increased pain, increased rigidity, severe nausea and vomiting, high fever, and an increase in the white blood count. If the indications are present, the common bile duct should be explored even though the gall bladder is acutely inflamed.

Cholecystectomy was performed in 9 per cent of the cases. In 83 per cent, stones were found in the common bile duct.

Edwards prefers a transverse incision for biliary operations. Anomalies of the ducts and vessels were discussed and lantern slides were shown illustrating the anomalies encountered in this series.

Claude S. Beck, Cleveland. **Pressures on the Heart.**—Heart action can be disturbed by (1) pressure, (2) angulation, (3) rotation.

Poition and angulation are poorly tolerated by the human heart. Dislocations of the heart, causing rotation and angulation, are sometimes the result of inflammatory disease of the mediastinum, therapeutic pneumothorax, or malformations of the chest wall. Operative intervention can correct such displacement.

Pressure on the heart can be classified as "acute" and "chronic." Beck prefers the term "acute pressure" to the generally used term of "tamponade."

The most common cause of acute pressure is stab wound of the heart. Spontaneous and traumatic ruptures of the auricles may occur following crushing chest injuries. Not all of these patients die suddenly. Some could be saved by operation.

Chronic earlie pressure can be either generalized or localized. Three cases were reported with compression scars over the right auricle and ventricle. Operative relief of these localized compressions was successful.

In another case, there was a ring of calcium deposited around the pulmonary artery which was removed surgically.

A case was reported in which the patient had a severe contusive injury of the chest. Later, he developed signs of compression of the heart and died. Autopsy revealed that the parietal pericardium had an opening in it. Both ventricles herniated through this opening and earlie compression resulted. Cure could have been obtained by replacing the heart in the pericardium and closing the opening in the pericardium.

A common cause of compression is generalized pericardial scarring. Beck has operated on fifty-seven such patients. 68.4 per cent of these are living and cured and two 15.3 per cent are improved. There were ten postoperative deaths—five from tuberculosis and five from other causes. There was only one operative death and this was due to ventricular fibrillation.

A case was reported in which there was a tumor mass in the wall of the left ventricle. The mass was the size of a tangerine. It had a calcified wall and the content was solidly packed debris without cellular morphology. The mass was successfully removed and the patient is living without symptoms.

Pericardial effusion may cause compression of the heart. If the fluid cannot be aspirated surgical internal drainage should be established into the left pleural cavity.

Norman F. Miller, Ann Arbor. **The Abuse of Pelvic Surgery in the Female.**—The divergent views held by physicians regarding the need for certain types of pelvic surgery plus the story told by the removal of countless organs now recognized as normal would indicate that some attention to this subject is in order.

It is important that the profession be aware of the following facts:

(1) The decreasing confidence manifested by patients in physicians when operation is advised. This may be a manifestation of the American custom of shopping, but some of it represents a true change in patient-physician relationship.

(2) In recent years there has been a marked increase in the incidence of pelvic surgery, as shown at daily hospital listings, in spite of new forms of chemotherapy, reduced birth trauma due to improved obstetrics, and a vastly increased knowledge concerning the functional changes in the female generative organs.

(3) During the war years, when civilian hospitals were filled to capacity, operating schedules rose to a new high and showed an increasing number of pelvic operations. Of course some of this increase can be attributed to insurance programs and to higher wages, but these factors do not explain all of the wartime increase.

(4) We are now in the midst of the greatest educational program for the development of surgical residencies in the history of medicine. We must not fail to recognize that the resulting abundance of surgical talent must also seek an outlet for its skill. In the careful screening of patients for conditions amenable to surgical treatment, it is imperative that there be available reasonable agreement as to what constitutes surgical disease.

In 1936, Carpenter analyzed 1137 gynecologic specimens from 11 general hospitals. In these specimens there were 314 excised ovaries. Pathologic examination of these specimens of ovaries revealed that 78.9 per cent of the ovaries were within normal physiologic limits. The changes which were present were as follows: follicle cyst, 57 per cent, simple cyst, 11.1 per cent, corpus luteum, 10.8 per cent.

It is important to recognize the fact that the normal functioning ovary varies in size. This alteration seldom exceeds 5 cm. Persistent enlargement beyond the normal 5 cm limit calls for removal.

In a study of 934 enlarged ovaries at the University of Michigan, in 1942, Miller noted that 49.3 per cent of the ovaries removed were under the 5 cm limit of normal. Further analysis of the 461 small ovarian tumors under 5 cm revealed that 96.9 per cent of these were of the simple type and removal was not justified.

In 1937, Cook reported 1378 cases of ovarian cysts of less than 7.5 cm. He observed that the vast majority of these were retention cysts and were of no clinical significance.

Mengert has reported a study of 1320 ovaries removed at one hospital. Of these, 99.3 (75 per cent) were normal or contained follicular or corpus luteum cysts.

Miller is of the opinion on the basis of his own experience and that of others, that there is little reason for oophorectomy on the basis of minor palpable cystic change. This does not apply to ovaries showing progressive increase in size beyond 7.5 cm nor to solid tumors of the ovary. Although oophorectomy is a simple surgical procedure no surgeon is properly equipped to perform this operation until he has thoroughly familiarized himself with the normal physiologic variations of the ovary.

The uterus also suffers from unjustified surgical annihilation. Here again failure to comprehend the full physiologic function of the organ is a factor. It is important to remember that the uterus serves both as a user and as a stimulator of ovarian hormones at a time in life when the cap of youth is running low. Premature removal of the normal uterus hastens atrophy and functional inactivity of the ovaries. Excision of the uterus in the absence of disease cannot be justified any more than the removal of the normal breast.

In a study of 246 hysterectomies at ten different hospitals in ten different communities in three middle western states, Miller discovered a none too happy picture. Approximately one half of these (43.9 per cent) were performed in patients between the ages of 40 to 49 years.

Sixty-six per cent were subtotal, 23 per cent total, and a per cent vaginal hysterectomies. In view of the enthusiasm and propaganda favoring the total operation, one might have expected a higher incidence of complete extirpation. It is Miller's opinion that the total operation is more difficult than the subtotal, other opinions to the contrary notwithstanding. Furthermore, except for the obvious fact that future disease of the cervix is eliminated, the other advantages sometimes claimed for complete hysterectomy still remain to be proved. He is unimpressed by the evidence presuming to prove a lower mortality and morbidity for the total operation. Total hysterectomy should certainly not be attempted by the occasional operator.

The leading symptom in this series of cases was excessive menstrual bleeding, 41.4 per cent of these patients presented this primary symptom. It is interesting to note that 17.4 per cent had no symptoms whatsoever.

The findings at pelvic examination prior to operation are of interest. 18.6 per cent had a perfectly normal pelvis at examination, in 31.7 per cent it was thought that uterine fibroids were present.

In the final studies of the specimens removed, the pathologist reported that 30.8 per cent of the organs excised revealed no microscopic evidence of disease. The figure is especially revealing since it included, as acceptable findings diseases of the adnexa, prolapse, hyperplasia of the endometrium, and pelvic relaxation. The fact that 17.4 per cent of the patients presented no symptoms and 18.6 per cent had no palpable pelvic disease does not of itself warrant the assumption that almost one fifth of the patients in this particular series had acute "remunerative" or "hip pocket" hysterectomies. However the discovery that 30.8 per cent were found to have no pathologic changes in the organs removed is not readily accounted for. Further correlation shows that 11, or 16.6 per cent, had neither symptoms, palpable pelvic disease, nor histopathology of the removed organs.

In 49.7 per cent of the patients the clinical diagnosis was confirmed. In 17.4 per cent the clinical diagnosis was not corroborated but the operation nevertheless considered justifiable. In 33.1 per cent there was either no disease or else disease contraindicating hysterectomy.

Even with the very liberal allowances permitted in this study Miller found that almost one-third of the extirpated uteri were absolutely free from evidence of disease. If this trend is borne out by further study it is time that the profession scrutinize the more commonly accepted indications for pelvic operation, especially oophorectomy or hysterectomy.

Thomas Leslie Lee, Ann Arbor and H. Fleming Fuller, Kingston, N. C. The Surgical Treatment of Intractable Dysmenorrhea.—There are two types of dysmenorrhea: (1) primary (functional) and (2) secondary (pathologic).

Preaerial sympathectomy is recommended only in the first type. Fifteen cases were reported in which preaerial sympathectomy had been performed. The results were uniformly good.

K. M. Brinkhous, Chapel Hill. Thrombin and Its Clinical Applications.—The mechanism of hemostasis was reviewed in detail. The time required for the various reactions in the process of hemostasis is of great importance. All thromboplastins are poor hemostatic agents because too much time is consumed in the formation of thrombin. This fact led to the idea of using preformed thrombin in hemostasis.

Brinkhous was a member of the research group at Iowa which did pioneer work in the purification of thrombin. He briefly reviewed the preparation of purified thrombin. Seegers has recently improved this method and obtained an extremely potent and practically pure thrombin. B-time thrombin which was used in these preparations has shown no antigenicity in man.

Thrombin solution directly applied to a bleeding surface is not efficient. It is necessary to spray the solution under high pressure from a needle and syringe.

The application of thrombin solution by cotton wicks saturated with the solution will control bleeding promptly but on removal of the cotton the clot is broken and bleeding starts again.

To obviate these difficulties soluble preparations have been introduced as a vehicle for thrombin. The best of these are fibrin foam and gelatin sponge. A third preparation, oxidized cellulose, is acid in reaction and will destroy some of the thrombin.

Local application of thrombin has been used widely in minor surgery, particularly in the control of arterial bleeding, bleeding in tumor beds and along venous sinuses. It also has

some and found in the control of

Gordon S. Fahrni, Winnipeg: **A Few Factors in Thyroid Surgery Influencing Morbidity and Mortality**—A series of 4951 cases, in which subtotal thyroidectomy was performed was analyzed. Of these, 2,430 were of the toxic diffuse type and 2,521 were nodular goiters (including the nontoxic, toxic and malignant goiters and chronic thyroiditis).

In toxic diffuse goiter, a radical removal of both thyroid lobes was carried out. In nodular goiter, a less radical resection was performed.

Lugol's solution was used preoperatively in all cases, whether obviously toxic or not. Since October, 1945, thiouracil has been used in the severe toxic cases. This drug is discontinued nine to ten days before operation and the patient carried on Lugol's solution until operation. Toxic patients are advised to take 3 to 5 minims of Lugol's solution twice weekly for several months following operation.

Forty-six patients have been operated upon for carcinoma, which is 0.9 per cent of the entire series and 1.9 per cent of the nodular goiters. Radical removal of the gland plus post-operative radiation is indicated in all such cases.

It is important that all patients with nodular goiters in which the patient has noticed an enlargement or increased firmness of the old goiter, be advised to have thyroidectomy because of the danger of malignancy.

Forty-four patients were operated upon during pregnancy. There were no miscarriages and all patients were carried through their pregnancies satisfactorily. Fahrni advises thyroidectomy during pregnancy as soon as the diagnosis is made, unless the disease should occur during the last trimester and be of relatively low grade toxicity.

The presence of heart disease with thyrotoxicosis is no contraindication to thyroidectomy. Such patients are greatly improved after thyroidectomy.

In toxic cases, it is important that the patient be gaining weight at the time of operation. Lugol's solution and thiouracil should be used judiciously. Unfortunately, many patients are given Lugol's solution for many months before being sent to a surgeon. Such patients are always very poor risks.

In the preparation of toxic cases for thyroidectomy, the patient should be allowed to be ambulatory.

The over all mortality was 0.7 per cent. In the toxic diffuse cases, the mortality was 1.1 per cent and in nodular goiters, the mortality was 0.3 per cent. The common causes of death were thyroid crisis, heart failure, pneumonia, and cerebral thrombosis. Other causes of death were hepatic failure, anesthesia surgical shock, and pulmonary embolus.

In the last 423 thyroidectomies, no deaths have occurred. In these cases thiouracil has been used in the more toxic cases.

R. B. McKnight, Charlotte: **An Analysis of 1160 Consecutive Thyroidectomies**.—In this series, there were five deaths, two in white and three in colored patients, an over all mortality of 0.45 per cent. This revealed a mortality rate of 0.2 per cent in white patients and 4.0 per cent in colored. There were no deaths in the severely toxic cases. He attributes this largely to the preoperative use of intravenous iodine in doses of 100 to 150 minims of Organidin in 1,000 c.c. of 10 per cent glucose given daily three to five days before operation. In the entire series there were no errors. Neither thiouracil nor any of the allied drugs was used in this series. The prevention, incidence, and management of such immediate complications as bilateral recurrent nerve injury, hemorrhage, parathyroid disturbance, psychosis, etc., were discussed.

Irvin Abell and Irvin Abell, Jr.: **Louisville Endometriosis. An Analysis of Personal Experience**.—Endometriosis may be divided into five groups (Sampson): (1) direct or primary endometriosis; (2) peritoneal or implantation endometriosis; (3) transplantation endometriosis; (4) metastatic endometriosis; (5) developmentally misplaced endometrial tissue. The history of endometriosis was reviewed in detail.

Abell and Abell, Jr., reported a case in which a catheter remained in the uterine cavity for four years without causing unusual symptoms. Perforation of the uterine wall then

occurred, and the catheter worked its way into the left ischio-rectal fossa. Eventually a sinus tract developed to the outside. Operative exploration revealed that endometrial implantation followed the course of the catheter. These implants were found in the entire fistulous tract from the uterus to the opening in the skin over the ischio-rectal fossa. The patient was cured by radical excision of the fistulous tract and removal of the catheter.

The choice of treatment is between deferred treatment, conservative surgery, and either surgical or radiation castration. The young woman who has been assured that no serious consequences will result from deferred operation, may, in the hope that the pelvic condition will subside or that she will become pregnant, prefer to suffer mild discomfort rather than accept the risk of surgical castration.

The young woman in whom operation is unavoidable, either in the longing for a child or the fear of premature menopause, may earnestly desire conservative surgery with its associated risk of a second laparotomy.

An older woman who can anticipate an early menopause may endure the disability with the expectation of its early termination. Upon the evaluation of such factors rests the policy of conservatism.

A series of 170 cases of endometriosis was reported. Only one patient under the age of 20 years was operated upon. The highest incidence was during the third decade. There were only fifty-one single women in the series, indicating that sterility is in some instances of no assistance in diagnosis. Of the 119 married women, 54, or 50 per cent, were childless, and of these 54 some 28 stated that they were unable to become pregnant.

There were 24 instances of acquired dysmenorrhea, 9 of menorrhagia and 5 of metrorrhagia. Thirty-three patients were completely symptomless, 14 of whom came in for physical examination and 19 because of enlargement of the abdomen.

The classical symptoms of acquired dysmenorrhea occurred only 24 times, of primary sterility but 23 times, and of characteristic pelvic pain in only 31 cases. In only 77 of the 170 cases did endometriosis occur alone. In 93 cases it was associated with other pelvic disease.

The affinity of this disease for the ovaries accounts, in part, for the surgical castration essential to a complete cure in 66 per cent of the reported cases. Cases seen in the early stages of the disease numbered only 31. In 4 of these an opportunity presented itself to observe the patient from the time of onset of pelvic pain and tenderness until the disease developed. The lesions were palpable after two, five, six, and twelve months.

Donald T. Imrie, Vicksburg: Osteomyelitis Today—At the present time there is an improved picture of osteomyelitis as the result of sulfanilamide and penicillin therapy. Indications for surgery are not completely agreed upon. The need for individualizing cases on the basis of "variable factors" as well as "basic common factors" was emphasized. The effect of penicillin on these factors was discussed with emphasis on early administration before thrombosis of the vessels has occurred and isolation of the bone from the general circulation. Large doses of penicillin are recommended. As much as 100,000 units of penicillin every three hours may be required because a certain amount of isolation of bone may already have occurred in spite of negative x-ray findings.

Roentgenograms were shown of a patient with staphylococcus septicemia and acute hematogenous osteomyelitis treated early enough to prevent actual bone necrosis. Another case showed sequestration but arrest of further necrosis. A third case revealed a low grade infection which required the drainage of a subperiosteal abscess. A fourth case exemplified the type of osteoplastic work done in the old chronic cases. Such radical surgery is made safe with penicillin.

Surgical intervention is rarely necessary in the acute cases except those in which subperiosteal abscess develop. The abscess should be evacuated and the wound may be closed if penicillin is given.

Casts or splints should be used only when necessary to facilitate healing of a pathologic fracture.

David B. Murphey, Tampa *The Use of Atmospheric Pressure in Obliterating Axillary Dead Space Following Radical Mastectomy*—After performing radical mastectomy, it is impossible to close the wound without trapping air beneath the skin flap. If this entrapped air is removed by aspiration following airtight closure of the skin, the skin flaps are pressed into contact with the underlying tissue by atmospheric pressure and this apposition will be maintained unless the vacuum is broken by an accumulation of fluid.

Before closure of the wound, a large (24 S) catheter containing multiple perforations is passed through a small stab wound, making a snug fit just anterior to the latissimus dorsi muscle, and its tip placed in the apex of the axilla, but not in contact with the vessels and nerves. The skin is then closed. A syringe is attached to the catheter and the air with drawn from the axilla. The skin flaps are immediately sucked into the axilla. The skin flaps are then arranged so that they fit smoothly into the axillary dead space. The catheter is tied and a dressing applied, leaving the arm free. Thereafter, the catheter is aspirated every twelve hours. Between aspirations, the catheter is tied to prevent the entry of air into the wound with elevation of the flaps. Continuous suction of the Wangensteen type was first used, but was abandoned due to a tendency for tissue to enter the perforations and obstruct the catheter when suction was maintained.

This method has been used successfully in twenty-five cases, and Murphey is of the opinion that it adequately obliterates all dead space, with minimal fibrosis.

T. C. Davison and A. H. Letton, Atlanta *Muscular Relaxation in Abdominal Surgery With the Use of Pentothal Oxygen and Curare*—Report of Over 1,000 Cases—A series of 1,000 abdominal cases, in which pentothal oxygen and curare anesthesia were used, was analyzed.

This is an efficient type of anesthesia for abdominal surgery and has certain advantages over spinal and inhalation anesthesia. There was no mortality in this series which could be directly attributed to the anesthesia.

William Milton Adams, Memphis *Free Grafting of the Nipples in Mammoplasty*—Adams presented an excellent motion picture demonstrating a technique for mammoplasty in which free grafting of the nipples is performed. An elliptical transverse incision is made first, excising the entire lower pendulous portion of the breast including the areola. In this way, the normal contour of the breast can be restored.

From the excised portion of the breast, the areola and nipple are then dissected free as a full thickness graft. After the original incision has been closed and the new contour of the breast is inspected, a small circular area of skin is removed from the proper place to apply the areola. The previously excised areola and nipple are then transplanted to this area as a graft and held in place by fine plastic suture material.

The end results of several of these cases were demonstrated, showing the excellent cosmetic effect obtained.

Harry D. Morris, New Orleans *Amputations About the Foot and Ankle Following Trauma*—This paper was based on 2,612 major amputations performed at an amputation center.

Amputations distal to the bases of the metatarsal bones are satisfactory because insertions of the leg muscles are preserved and the balance of the foot is maintained. However, often this amputation cannot be performed because adequate planter flaps are not available. Such a transmetatarsal amputation necessitates a special prosthesis.

The Lafranc, Chopart, Ricard, Boyd, and the Pirogoff amputation techniques through the posterior part of the foot have many disadvantages.

Morris devised a modification of the Chopart technique for posterior foot amputation. This technique was partially based on the report of Vasconcelos, in 1937.

Eight cases were operated on according to this technique. In four of these cases, reamputation was necessary. Morris felt certain that the other four patients would have done better with a Syme amputation or an ideal below the knee stump.

opened and the catheter worked its way into the left subdermal space. Eventually a contrast developed to the outside. Operative exploration revealed that external implants had followed the course of the catheter. These implants were found in the same fashion from the scars to the opening in the skin over the subdermal space. The patient was cured by radical excision of the fistulous tract and removal of the catheter.

The choice of treatment is between deferred treatment, conservative surgery and either surgical or radical excision. The young woman who has been assured that no serious consequences will result from deferred operation, may, in the hope that the pelvic infection will subside or that she will become pregnant, prefer to suffer still discomfort as she has among the risk of surgical excision.

The young woman in whom operation is more liable either in the bearing for a child or the fear of premature menopause may extremely desire conservative surgery with its associated risk of a second laparotomy.

In older women who can anticipate an early menopause may exclude the doubtless in the expectation of its early termination. Upon the evaluation of each case depends the policy of management.

A series of 143 cases of ectopic pregnancy was reported. Only one patient under the age of 20 years was operated upon. The highest incidence was during the third decade. There were only fifteen single women in the series indicating that childbearing is in some instances of an advantage in diagnosis. Of the 119 married women, 54 or 45 per cent, were stillborn and of these 54 were so stated that they were unable to become pregnant.

There were 31 instances of acquired dysmenorrhea, 9 of menorrhagia and 5 of metrorrhagia. Thirteen patients were completely asymptomatic 14 of whom came in for physical examination and 19 because of enlargement of the abdomen.

The clinical symptoms of acquired dysmenorrhea occurred only 24 times of primary menorrhagia 24 times and of characteristic pelvic pain in only 31 cases. In only 7 of the 143 cases did ectopic pregnancy occur alone. In 92 cases it was associated with a low pelvic infection.

The effect of this disease for the ovarian arteries is part for the surgical excision essential to a cure in more than 60 per cent of the reported cases. Cases seen in the early stages of the disease required only 31. In 4 of these an opportunity presented itself to change the patient from the time of onset of pelvic pain and treatment until the mass developed. The lesions were palpable after two, five, six and twelve months.

Donald T. Linn, Linköping. Osteomyelitis Today.—At the present time there is as improved picture of osteomyelitis as the result of collaboration and personal efforts. In various for surgery are not every case agreed upon. The need for individualizing cases on the basis of variable factors as well as basic common factors was emphasized. The effect of penicillin on these factors was discussed with emphasis on early administration before thrombosis of the vessels has occurred and isolation of the bone from the general circulation. Large doses of penicillin are recommended, as much as 10,000 units of penicillin every three hours may be required because a certain amount of infection of bone may already have occurred in spite of negative x-ray findings.

Enostosis was shown of a patient with staphylococcus septicaemia and acute haematogenous osteomyelitis treated early enough to prevent actual bone necrosis. Another case showed sequestration but arrest of further necrosis. A third case remained a low grade infection which required the drainage of a subperiosteal abscess. A fourth case exemplified the type of osteomyelitis work done in the old chronic cases. Most radical surgery is made possible by penicillin.

Surgical intervention is rather summary in the acute cases except those in which sequestra are shown directly. The abscess should be drained and the wound may be closed if penicillin is given.

Case excisions should be made only when necessary to save the bone and not as a palliative measure.

One difficult in curbing can be in the so the term I t l States is the fact that in only three state are records of can r contr l kept These are Lou and Georgia and M pp

William F. Riesenhoff: It is more Carcinoma of the Lung Diagnosis and Treatment
Over a thirteen year period 3 cases of carcinoma of the lung are reported. The study
not include the clinically inoperable case. The clinical picture is a malignant neoplasm
on the lung tissue and more frequent in males than females. The right and left lung are involved
approximately the same.

The age of the tumor did not vary from the usual age of other malignant neoplasms. Age seemed to offer no contraindication to operation.

Cough was the chief symptom in 1 per cent. Other symptoms were as follows: hemoptysis 63 per cent, pain 50 per cent, loss of weight 39 per cent, hyperpnea 23 per cent, pneumonia 18 per cent, fever 13 per cent, and night sweats the least 3 per cent. The more common symptoms were included in at least 1. There were no pathognomonic signs or symptoms of primary carcinoma of the lung. The clinical picture was as varied as any common pulmonary disorder.

In this case the roentgenogram reveals a small nodule in the right upper lobe. This is the most important method of examination. Second to roentgenograms in importance is bronchoscopy. In 10 per cent biopsy findings are positive. A pulmonary new growth in the periphery or confined to the upper lobe bronchus can be detected by bronchoscopy. Bronchoscopy can only reveal a lesion if the bronchus is a small growth. It may not produce a shadow on the x-ray plate. A positive biopsy is often difficult to interpret and is of doubtful danger.

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In this series the tumors correlated or adjacent to the lila in the majority of cases. A norty oeu re] n per phe. The method of spread and cause] The e gro th a ng a the per plery re e ften a pto nat

In 0 per cent of the 11 patients who had a pneumonectomy metastases to the bronchial and tracheal lymph nodes was found. In the 11 overall cases metastases to regional lymph nodes of the thorax were found in the following organs: 4 in the supraclavicular and axillary lymph nodes, 1 in the pleura, 1 in the lung, and 1 in the contralateral lung on the same side as the primary tumor. In 4 of the 11 patients, metastases were found in the skin and subcutaneous tissue.

Fifty five per cent of the adenocarcinomas were squamous cell carcinomas and 34 per cent were adenocarcinomas.

Penicillin and sulfonamide are also used preoperatively. An important place of prophylactic treatment is the prophylaxis of pneumonia. The advantage of pneumothorax are (1) that a therapeutic test is made with the patient. (2) tolerate removal of one lung, (3) the size of the lung is reduced so that a planned handling of the structure at operation is easier. (4) the patient is learned to breathe with one lung and thus avoids a certain degree of pleural shock. (5) the blood flow through the collapsed lung is reduced and therefore the strain on the right heart to lift a great blood flow through one pulmonary artery is greatly reduced. (6) the location of the growth regarding the position relative to the mediastinum of the pleural cavity is foreknown more accurately.

Total pneumonectomy is the only effective method of treatment of pulmonary carcinoma.

The details of operative technique are illustrated. An anterior approach is preferred. In addition, the pulmonary artery is the first step. Removal of the bronchial stump by the use of mattress suture of interrupted silk or cotton placed through the bronchial stump in a manner that the posterior or medial anastomosis approximated to the anterior or lateral anastomosis. All some hat proximal to the end of the resected stump thus creating a variable area from 1 to 2 cm. distal to the suture line. A flap of parietal pleura should be sutured over the end of the stump of the bronchus.

The Syme amputation offers the best solution to the problem of amputation of the foot proximal to the metatarsal bone. Morris reviewed forty-two personal cases in which the Syme amputation had been performed. Subperiosteal resection of the calcaneus is preferred because there is less danger of injuring the blood supply of the flap. In only two of these cases was reamputation necessary.

One of the patients with reamputation had Ruenger's disease. This was an error in clinical judgment and the patient should never have had a foot amputation. In the other patient, reamputation was necessary due to a defective plantar flap and not due to any fundamental shortcoming of the operative procedure itself.

Arnold S. Jackson, Madison. Probacil, in the Treatment of Hyperthyroidism.—All patients with hyperthyroidism observed by Jackson during the last year have been treated with propylthiouracil. A study of seventy patients so treated was reported. Thiouracil was discontinued entirely and supplanted by propylthiouracil, which appears to be more effective and far less dangerous. In only one case did the white blood cells count fall below 5,000, and there was no reaction observed in this instance.

At present five children with exophthalmic goiter, all between the ages of 7 and 14, are receiving the drug. The basal metabolic rate has returned to normal in each instance. They have all gained an average of twelve pounds in weight and have been able to resume their schoolwork. When they have been on treatment twelve months, the drug will be discontinued with the hope that a cure will be effected. Jackson feels that propylthiouracil has been used for too short a time for anyone to say definitely that a cure may or may not be effected by its use in exophthalmic goiter.

It has been very advantageous in the preoperative preparation of complicated cases of multiple toxic adenoma. Patients with advanced cardiovascular disease, diabetes, and marked weight and strength loss have shown a remarkable response to treatment. With the use of this drug the heart condition is improved, the basal metabolism returns to normal, and thyroidectomy can be performed in one stage.

A compilation of cases from other physicians shows that approximately 1,500 patients with hyperthyroidism have now been treated with propylthiouracil. Only one case of agranulocytosis occurred, and that patient recovered.

Ooyle Crutchfield, University. Surgical Treatment of Hypertension.—Crutchfield reported on 156 cases in which splanchnic nerve resections had been done for hypertension. He stated that in eighty-one of these cases the results were good and the patients have been able to return to some form of gainful occupation. The importance of careful selection of patients for this operative procedure was emphasized. Crutchfield stressed the fact that he did not believe the procedure adaptable to all patients who have an elevated arterial tension and he believes that the end results can be greatly improved if the patients are more carefully selected.

John A. Martin, Montgomery. The Problem of Carcinoma of the Colon in the Southeast.—This presentation was a statistical study of the occurrence of carcinoma of the colon in the southeastern states. There is no statistical evidence to indicate that any great progress has been made in the early recognition of carcinoma of the colon in spite of recent educational campaigns.

The following are the reasons for the delay in the diagnosis and treatment of cancer of the colon: (1) failure on the patient's part to seek early medical aid; (2) failure of the physician to recognize early carcinoma; (3) physicians first consulted incapable of making early diagnosis or rendering the best service possible; (4) incorrect advice from physicians; and delay in receiving a separate treatment after the diagnosis is made.

Martin emphasized the fact that if a similar system of physical and x-ray examinations now used in the diagnosis and treatment of tuberculosis were to be applied to cancer of the colon, the mortality of this disease would fall in a manner similar to that of tuberculosis.

loss of bone surface from high velocity bullets or shrapnel, (4) incompletely reduced fractures or those in which there was interposition of soft tissue, (5) improper and ineffectual fixation after reduction, (6) improper use of external fixation pin units.

Careful preoperative care is important. Wounds connected with the fracture must be eliminated. Sequestra and foreign bodies should be removed. Soft tissue defects should be previously covered with skin grafts.

Since the advent of chemotherapy, the waiting period, from the time drainage ceases until the bone grafting, has been cut down from the usual six months to two years, to approximately eight weeks.

This waiting period can be adequately used by instituting physiotherapy, exercises, and massage. Casts or braces should not be kept on unless they maintain length. The patient's general condition should be investigated, and for twenty-four hours prior to operation, penicillin is administered.

Rankin prefers spinal anesthesia in the lower extremities, pentothal in the upper extremities, and endotracheal gas anesthesia for the mandible. During the operation, the patient should be supported with infusions and blood.

Rigid operating room technique is insisted upon. Fine cotton sutures are used.

The periosteum should be disturbed as little as possible. All scar tissue is removed from the end of the bone and the medullary cavity is widely opened. Screws retaining the grafts in position should be placed as far from the fracture site as possible and must traverse both cortices. A complete débridement is performed. The wound is dusted with sulfamizide. All dead space is eliminated and the skin is closed with interrupted cotton sutures.

Many types of grafts were used in this series. Sliding inlay grafts were used principally in fractures of the humerus, femur and tibia.

An attempt was always made to use at least one third of the circumference of the shaft of the bone, so that there was a large, sturdy osseous bridge across the line of fracture.

Fractures of the clavicle with either nonunion or bony defects heal rapidly with the use of the split rib technique.

Thoracic cage defects were repaired by subperiosteal removal of alternate ribs from the opposite side of the chest. One end of the transplant was sutured to the rib end with steel wire and the periosteum closed around it. The other end was wedged to a longitudinal split in the sternum and fixed with steel wire.

All patients were subsequently placed in padded plaster casts. Penicillin was given for a period of ten days. Sulfadiazine was sometimes added.

The distribution of grafts in this series was as follows: mandible, 6, clavicle, 4, humerus, 7, radius, 16, ulna, 13, radius and ulna combined, 9, scaphoid, 10, thoracic cage defects, 3, femur, 10, tibia, 18, internal malleolus, 1.

In four cases of the originally compound fractures, a small pocket of pus was encountered at the time of operation even though there was no drainage. In all of these cases, the bone graft operation was performed and the wound was closed. Large doses of sulfadiazine were given and 100,000 units of penicillin were administered every three hours. One of the wounds healed by primary union. Two drained, but eventually healed with preservation of the graft and union of the fracture. In the fourth case, a graft of the radius was lost. At a later date, another graft was successfully applied to the radius.

Of the ten ununited scaphoid fractures six healed with bony union. There were four in which there was no union but apparently enough fibrous union occurred so that these men could return to limited duty status. There was only one case in which a fracture of the tibia occurred following removal of the bone graft, and this was approximately ten weeks following operation. All patients who had grafts removed from the tibia were immobilized in a cast or brace for two to three months.

J. A. Cunningham, Birmingham. Hidradenomas of the Vulva, Report of Five Cases.—The possible relationship between hidradenoma and carcinoma of the breast was discussed.

At the end of the operation, 150,000 units of penicillin are introduced into the thoracic cavity. The trapped air is removed by leaving an aspirating catheter in the wound during closure. No postoperative drainage of the pleural cavity is necessary. If gross infection of the lung is present, 50,000 units of penicillin are introduced daily into the thoracic cavity, in addition to parenteral chemotherapy. No instances of empyema have been encountered.

In this series, from 1933 to 1939, there were 30 cases with 8 deaths (27 per cent). From 1940 through half of 1946, 82 patients were operated upon with 17 deaths (20.7 per cent). The total operative mortality was 22 per cent.

Marshall L. Michel, New Orleans. *Acute Malignant Obstruction of the Colon*.—A series of 55 cases was reviewed from Charity Hospital and Touro Infirmary, in New Orleans. The over all mortality was 33 per cent. The cases were handled by twenty-five different surgeons. The maximum number of cases done by one surgeon was eight. The incidence of complete acute obstruction in all cases of carcinoma of the colon admitted was approximately 27 per cent.

The fact that the patient with malignant obstruction of the colon is in double jeopardy, first, from the obstruction and, second, from the malignant disease is important. The treatment of the obstruction is of primary importance, and the removal of the malignant growth should be postponed until a later date.

Acute obstruction of the colon often results in a closed loop obstruction. Perforation of the colon is a complication to be feared and occurred in eight of these fifty-five cases. Only two of these perforations occurred in the cecum.

In forty-one of the fifty-five cases, the obstruction occurred on the left side of the colon. The mortality rate was higher on the right side.

In a number of these cases, signs of acute obstruction were the first manifestation of the malignant disease. The importance of x-ray studies was emphasized. Both a flat plate of the abdomen and emergency barium enema should be performed in order to localize definitely the site of obstruction so that abdominal exploration can be cut down to a minimum.

Delay of surgical therapy of acute obstruction of the colon and attempts at conservative treatment greatly jeopardize the patient's chances of recovery. The Miller Abbott tube is of no value in the treatment of obstruction of the large intestine.

In obstruction of the left colon, a simple loop colostomy of the right transverse colon is the procedure of choice although cecostomy also gives good results.

In acute obstruction of the right side of the colon, the procedure of choice lies between cecostomy, ileotransverse colostomy, ileostomy or combination of ileostomy and ileotransverse colostomy.

E. Murphy Howard, Harbin, K. *Obligations and Opportunities in Industrial Surgery*.—Howard pointed out that 90 per cent of industrial plants fall into the small plant category (500 workers or less). Accident frequencies run to 62 per cent higher than in large plants, yet they are unable to afford the medical and surgical staff which big industries employ as a matter of course.

Howard recommended that small plant medical cooperative be formed. Pay roll deduction prepayments by the worker is the only solution in sight for this particular problem. Such plans are in effect in Pennsylvania, New York, Connecticut and California.

The opportunities of industrial surgery were enumerated. The industrial surgeon must serve as internist, surgeon, orthopedist, toxicologist, radiologist and psychiatrist. Therefore, his previous training should be of a general nature with particular emphasis on surgery and traumatology.

J. O. Rankin, Wheeling. *The Management of the Ununited Fracture*.—This presentation was based on 100 bone graft operations at a Naval hospital.

The following factors were responsible for the necessity of bone grafting procedures: (1) compound fractures in which proper and adequate debridement was not done; (2) compound fractures in which the patient was not seen in time by the surgeon to do a proper debridement; (3) relative frequency of compound comminuted fractures or fractures with

pulmonary structure were then enumerated, with particular emphasis on the location of the various bronchi and blood vessels.

The objections to the clamp and suture method are: (1) it is impossible to place the clamps precisely in the intersegmental plane, (2) the application of clamps across the lung tissue is crude and traumatizing, (3) excessive suture material is necessary predisposing the patient to secondary infection and foreign body reaction, (4) puckering and reduction in the size of the remaining segments is produced.

Pulmonary segmental resection according to the technique of Woods and Overholt was discussed in detail. All of the hilar structures of each segment are identified and divided prior to dissection of the intersegmental plane. These structures are the bronchus, the pulmonary artery, veins, and visceral pleura. Then the dissection is carried along the intersegmental plane through which the bronchi do not traverse and for practical purposes which plane is avascular. Prompt healing of the denuded lung surface follows and air leakage is of negligible importance.

Woods and Overholt have adopted the face down position with the diseased side dependent for pulmonary resection. They reported twenty-three segmental resections performed on twenty-one patients for primary bronchiectasis. No deaths have occurred. Bilateral lesions were present in eleven cases.

The incidence of complications is somewhat higher than those following lobectomy. A reduction of complications will probably follow wider use of this procedure. The preservation of pulmonary tissue is important.

Milton A. Gilmore, Parkersburg, W. Va. **The Control of Hemorrhage in Otolaryngology**—Hemorrhage from the ear is usually of a minor nature. Occasionally, however, as the result of extensive skull fractures in this region, hemorrhage from the ear may be severe. The treatment of choice is packing. Occasionally marked hemorrhage may occur from the lateral sinus during mastoidectomy. Here again tight packing is the treatment of choice. The use of the newly developed hemostatic agents in conjunction with the pack is also a worthwhile procedure.

Hemorrhage from the nose is the most common type dealt with in otolaryngology. These cases may be divided into two main groups: (1) local and (2) systemic. In handling of an acute massive nasal hemorrhage suction should be used to clear out the blood and definitely determine the bleeding point. Occasionally cauterization of the bleeding point may stop the hemorrhage. However, in many cases packing is necessary. Packing with moist packs soaked in adrenalin solution is still an efficacious method and the use of a local anesthetic is often indicated. Recently the use of cotton tampons immersed in thrombolytic solution has proved to be superior to any type of nasal pack.

It is necessary to pack the posterior part of the nares on rare occasions. When this is done the pack should always be removed in a period of forty-eight hours. Fracture into the posterior part of the nares may be extremely severe following basal skull fracture. In the most severe form of nasal hemorrhage ligation of the external common carotid may be necessary. Gilmore then discussed in detail the various arteries which supply different parts of the nose and mentioned in detail his own technique for ligation of the ethmoidal arteries by a transorbital approach.

Atropharyngeal hemorrhage occasionally presents a problem to the otolaryngologist. Hemorrhage here may be the result of trauma but most often is post-tonsillectomy. The most serious type of atropharyngeal hemorrhage is that which occurs in conjunction with infection. Usually it is impossible to stop this type of hemorrhage and ligation of the common carotid is frequently necessary.

Post-tonsillectomy hemorrhage is of two types: (1) primary and (2) secondary. The primary type of hemorrhage occurs immediately following tonsillectomy. *Notocain* and *thrombin* should be used and each bleeding point should be carefully isolated, clamped, and ligated. Gilmore strongly opposes sewing the tonsil pillars together in order to bring about

control of the hemorrhage. He is also of the opinion that local applications are of little or no use.

Secondary post tonsillectomy hemorrhage is usually not as massive but is often difficult to control because of the secondary infection. He is of the opinion that the use of lozenges which contain the sulfa drugs or penicillin is worth while in post tonsillectomy cases in order to prevent secondary infection.

Hemorrhage from esophageal varices is a difficult problem. Electrocoagulation and injections of sodium morrhuate have been advocated, but have been used with very little success.

Hemorrhage from carcinoma of the esophagus is difficult to control. Electrocoagulation and implantation of radon seeds are occasionally of value. Foreign bodies of the esophagus, peptic ulcers, or tuberculous ulceration may ulcerate through the walls of the esophagus and erode blood vessels, causing massive hemorrhage.

Hemorrhage from the tracheobronchial tree is extremely common. There are many different causes. Gilmore did not go into detail of the various causes of such hemorrhage, but mentioned several of the most common. Hemangioma of the bronchial tree is somewhat more common than generally believed and often such hemorrhage can be controlled by simple coagulation through the bronchoscope.

Joseph St. Stewart, Miami: **Extrinsic Duodenal Obstruction in the Newborn.**—Stewart reviewed from the literature forty-two such cases occurring in children under 5 years of age. Of these cases, 40 per cent were un diagnosed. He stressed the recent work of Ladd and Gross, who have shown how embryologic anomalies result in pressure on the duodenum, producing obstruction. The embryology of intestinal rotation was then discussed. The various anomalies were demonstrated by slides showing how it is possible for such anomalies to produce extrinsic pressure on the duodenum.

Stewart then reported two cases of obstruction of the second part of the duodenum due to the hepatic flexure of the colon lying over the duodenum in an incompletely rotated colon.

In one of these cases, the diagnosis was made correctly and operation produced immediate relief. In the second case the patient had had a previous laparotomy and appendectomy with no relief. Subsequent operation revealed the true nature of the obstruction and cause of abdominal symptoms. Mobilization of the right half of the transverse colon and relief of pressure on the duodenum produced complete relief of symptoms.

D. F. Hall, Louisville: **Biliary Peritonitis.**—There are four causes of bile peritonitis: (1) gall bladder disease, (2) defect or perforations of the bile duct, (3) trauma, and (4) congenital defects. Hall then demonstrated how each of these conditions could produce bile peritonitis and also discussed the signs and symptoms of bile peritonitis.

The possibility of bile peritonitis occurring in cases in which actual perforation of the gall bladder or ducts is not present must be kept in mind. If obstruction of the common bile duct and cystic duct is present, the back pressure in the gall bladder may be such as to cause a so-called "awerting" gall bladder. The result is extravasation of bile through the wall of the gall bladder into the peritoneal cavity, producing a bile peritonitis without actual perforation in the biliary tree.

Duncan McEwan, Orlando: **Mistaken Surgical Diagnoses in Hookworm Disease.**—McEwan analyzed a series of fifty-six patients admitted to his surgical service with abdominal pain. In 50 per cent of these cases, hookworms were found to be present in the stool, and specific therapy brought about complete relief of the abdominal symptoms. McEwan then discussed in detail the life cycle of the hookworm and stressed particularly the difference between the Asiatic hookworm and the species found in North America. Details of the pathology of hookworm enteritis were demonstrated, and it was emphasized how these patients may complain of abdominal pain. The presence of the enteric lesions in the ileocecal region may produce pain in the lower right quadrant, simulating appendicitis.

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STREPTOMYCIN IN SURGICAL INFECTIONS

IV PERITONITIS

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DURING the past ten years the mortality in peritonitis of various origins has been progressively lowered. Part of the reduction is undoubtedly to be attributed to the introduction and general use of increasingly more effective antibacterial agents. The sulfonamide drugs, penicillin, and streptomycin are however by no means solely responsible for the reduced mortality. The period in which these agents were coming into general use coincides with the period in which other adjuvant measures were also coming into general use and were being employed rationally as well as consistently. The routine management of peritonitis now includes in addition to chemotherapy and antibiotic therapy constant intestinal decompression, correction of perversions of the fluid and electrolyte balance, anticipation and correction of protein depletion and measures to prevent as well as to treat thrombophlebitis and phlebothrombosis with threatening pulmonary infarction and embolism. All of these measures play an extremely important part in the reduced mortality of peritonitis and they must be borne in mind in the evaluation of new forms of chemotherapy or antibiotic therapy.

ETIOLOGY OF PERITONITIS

Except in very young children peritonitis due to a single organism is relatively uncommon. The microorganisms responsible for this type of the disease are chiefly the beta hemolytic streptococcus group A, the pneumococcus and the gonococcus. The sulfonamide drugs and penicillin are effective against these microorganisms and the mortality in this type of peritonitis has been correspondingly reduced as a result of their use. In peritonitis due to perforation of the hollow viscera which is almost always associated with mechanical irritation a polybacterial infection is the rule comprising a variety of aerobic

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and anaerobic bacteria. Early studies¹ which indicated that peritoneal suppuration of fecal origin is due to the synergistic action of several bacterial species were later confirmed by Altmeier.² In an investigation of the bacterial flora of 100 cases of peritonitis of appendiceal origin, he was able to isolate an average of five different species of organisms from single peritoneal exudates. In some instances he isolated as many as sixteen different species. The microorganisms most commonly found, in association with other organisms which normally inhabit the gastrointestinal tract were *Escherichia coli*, aerobic and anaerobic nonhemolytic streptococci and Clostridia. Altmeier's experiments proved convincingly that *Esch. coli* was not the etiologic factor in peritonitis of appendiceal origin and also showed that it is not responsible for the odor of the exudate, as is commonly supposed. Previous studies³ have showed that streptomycin has a potent antibacterial action on a wide variety of gram negative and gram positive organisms, particularly those of gastrointestinal origin. Studies of Pulaski and Sprinz,⁴ which confirm the work of others,^{5,6} indicate that the drug diffuses readily into the peritoneal cavity in therapeutically effective concentrations following its parenteral administration. It might therefore, be expected that this particular antibiotic would have a potent therapeutic effect in peritonitis of polibacterial etiology.

EARLIER STUDIES ON CHEMOTHERAPEUTIC AND ANTIBIOTIC AGENTS

Experimental—By ligating and then opening the appendix Zintel and his associates⁷ produced peritonitis in three series of dogs, each series consisting of fifteen animals. In the first series, which served as a control series, only one of the fifteen animals survived. In the second series, in which treatment consisted of large doses of streptomycin given intramuscularly, there were four survivors. In the third series in which treatment consisted of a combination of penicillin intramuscularly and sodium sulfadiazine intravenously there were six survivors. These authors concluded that while streptomycin exerts a beneficial influence in experimental peritonitis in dogs the therapeutic results are not as good as when a combination of penicillin and sulfadiazine is employed.

Silman and his associates⁸ who carried out a similar experiment concluded (1) that streptomycin has no demonstrable suppressive effect on the bacterial flora of the peritoneal exudate and that it is of little value either as a prophylactic or a therapeutic agent in peritonitis in dogs, (2) that sodium sulfadiazine in large doses by the intravenous route also does not appreciably alter the bacterial flora of the peritoneum and has little or no protective effect against peritonitis in dogs (3) that penicillin in large doses (equivalent to 1,500,000 units per day in man) effectively eradicates gram positive bacteria. A significant number of the animals in the penicillin treated group survived. In these dogs the residual bacterial component which consisted chiefly of gram negative bacteria, was relatively noninvasive and disappeared spontaneously.

Clinical—The extensive literature on sulfonamide therapy may be summed up in the statement that most observers report some beneficial effects from its

ancillary employment in spreading peritonitis, but only equivocal results in cases in which there is considerable tissue necrosis or in which the microorganisms have localized due to abscess formation. Crile's report⁹ that penicillin in massive doses by the intramuscular route is strikingly effective in peritonitis of appendical origin has been confirmed by Brown.¹⁰

To date only a few reports have been made on the use of streptomycin in the treatment of peritonitis. Ilrshfeld and his associates¹¹ used it in twelve cases in eight of which penicillin or the sulfonamides were used also. They attributed the absence of spectacular results to the inability of streptomycin to suppress certain gram positive organisms, particularly the nonsporulating anaerobes. The report of the National Research Council on streptomycin¹² in the treatment of various infections included fifty three cases of peritonitis due, in order of decreasing frequency, to appendicitis, postoperative infection, diverticulitis, intussusception, cancer, salpingitis and abortion. Thirty nine of the fifty three patients recovered and twelve died. Of twenty one patients who received streptomycin and 'other forms of chemotherapy at the same time,' eighteen recovered and three died. It was the opinion of the Council that these results were sufficiently encouraging to justify the advice that streptomycin be used in all cases of peritonitis in which the infecting microorganism was susceptible. The dosage advised was at least 2 Gm. per day for five days or longer.

ANALYSIS OF CASES

The sixty three cases of peritonitis reported in this communication have been observed since November 1945. They form a heterogeneous group in respect to etiology, management, scheme of dosage, and duration of therapy. All of the patients were desperately ill but they were predominantly young males in good health, either on active duty or recently separated from military service and their nutritional status was usually excellent. The age range was from 7 to 62 years. Thirty nine patients were between 17 and 30 years of age, and only six were over 45 years of age. One would expect good resistance to infection in such a group.

The majority of patients in addition to streptomycin had intensive supportive therapy including constant intestinal decompression.

The results of therapy in twenty one cases of peritonitis in which only streptomycin was used are presented in Table I. In Table II are presented the results of therapy in forty two other cases in which streptomycin therapy was combined with penicillin therapy and, in some instances, with the administration of sulfadiazine also. Of the sixty three patients, five died and eighteen others either showed no results at all from streptomycin therapy or showed improvement only when other therapeutic methods were employed, such as drainage of a periappendical abscess.

There are no control cases in this series. Results are stated entirely from the standpoint of whether or not they could be attributed to the use of streptomycin. A patient was regarded as benefited by it if he had the type of rapid uncomplicated convalescence which could scarcely have been hoped for in the light of the disease process.

APPENDICAL PERITONITIS

Of thirty nine patients with peritonitis of appendical origin, seventeen had spreading peritonitis and twenty two localized peritonitis (Tables I and II). One patient with spreading peritonitis and one with localized peritonitis died, both were treated only with streptomycin. The patient with spreading peritonitis was a 49 year old man with severe diabetes mellitus and arteriosclerotic heart disease. Streptomycin was not regarded as effective because his improvement was slow clinically and subjectively. He died suddenly on the seventh postoperative day as the result of pulmonary infarction. He had received 0.25 Gm of streptomycin intramuscularly every four hours which is a relatively small dose.

The other death in this group occurred in a 58 year old white man with localizing peritonitis and an appendical abscess. He had a vascular accident on the first postoperative day, manifested by coma, stiff neck and jacksonian convulsions. He died on the seventh postoperative day, autopsy revealed a recent subarachnoid hemorrhage and bilateral pulmonary tuberculosis. There was a thick abscess wall about the drainage tube. The general peritoneal cavity was free from infection. He had received 0.25 Gm of streptomycin intramuscularly every three hours from the time of operation until death. It should

TABLE I RESULTS OF STREPTOMYCIN THERAPY IN TWENTY ONE CASES OF PERITONITIS

NUMBER OF CASES	SOURCE OF INFECTION	TYPE	DAYS TREATED	DAILY DOSE (IN Gm.)	RESULT
3	Appendicitis	Spreading	8	*0	Good rapid uneventful convalescence in each instance
1	Appendicitis*	Spreading	14	40	Good mass completely disappeared in ten days
1	Appendicitis	Spreading	"	15	Doubtful slow unspectacular improvement death from pulmonary infarct
4	Appendicitis	Localizing	10	14	Good in 2 cases Equivocal in 1 case with palpable mass
5	Appendicitis	Localizing	13	10	Doubtful in 1 case death from subarachnoid hemorrhage
2	Perforated carcinoma of sigmoid drainage abdominal perineal resection	Spreading	13	24	Good rapid localization and elimination of the infection
3	Volvulus, post anastomotic fistula of colon, perforated duodenal ulcer, operation	Localizing	9	10	Doubtful in all peritonitis minimal in volvulus improvement in others coincident with surgical drainage
1	Pelvic inflammatory disease	Localizing	14	10	Doubtful slow steady improvement
1	Gunshot wounds multiple	Spreading	1	10	1 or death from sepsis

*No operation.

TABLE II. RESULTS OF STREPTOMYCIN-PENICILLIN THERAPY (WITH AND WITHOUT SULFADIAZINE) IN FORTY-TWO CASES OF PERITONITIS

NUMBER OF CASES	SOURCE OF INFECTION	TYPE	STREPTOMYCIN*		PENICILLIN* (UNITS X 1000)			SULFADIAZINE† (NUMBER OF CASES)	RESULT
			DOSE (IN GM.)	DAYS TREATED (AVERAGE)	120 TO 210	250 TO 499	500 TO 800		
6	Appendiceal	Spreading	40	7	4	—	—	1	Good in all 1 pelvic abscess with absorption 1 trivial wound infection
4	Appendiceal	Spreading	30	12	—	1	1	1	Good in all, dramatic result in 1 nonsurgical case 2 patients had myocardial disease
2	Appendiceal	Spreading	30	10	—	1	1	—	Good previous therapy ineffective
4	Appendiceal	Localizing	24	7	1	2	1	—	Good in 2 nonsurgical cases ‡ doubtful in 2 cases recovery unspectacular
1	Appendiceal	Localizing	20	10	—	—	1	—	Good‡
8	Appendiceal	Localizing	15	14	4	3	1	2	Good in 5 cases Poor in 3 cases though no complications occurred dosages small
4	Perforated appendix duodenum	—	30 10	26	—	4	—	—	Good 1 patient treated without operation
3	Ileum	—	24	—	3	—	—	1	Good in 2 cases Doubtful in 1 case due to pulmonary complications
3	Colon	—	40 20	9	1	2	—	1	Excellent 2 perforations of sigmoid 1 post operative peritonitis
5	Multiple gunshot & stab wounds	—	40 06	11	5	—	—	4	Poor 2 deaths from nonbacterial causes 2 wound disruptions 1 pelvic abscess 1 unspectacular recovery All dosages small
2	Parametritis	—	24 16	11	1	—	—	1	Dramatic

*Daily dosage

†Daily dosage 6 Gm.

‡After addition of streptomycin to other therapy

be noted that the vascular accident which was responsible for his death occurred within twenty-four hours of operation.

In the patients who responded to therapy the clinical course was strikingly similar. In each instance the infection was controlled very rapidly. Distention and rigidity gradually subsided, ileus disappeared, and in all instances by the fourth day after operation there was passage of gas per rectum. Progressive localization of the process to the right lower quadrant of the abdomen or to the pelvis was notable. By the fourth or fifth day after operation the patient was free of discomfort and was on a selected diet. By the tenth day the temperature and pulse were normal.

The three patients treated without operation recovered as rapidly and as uneventfully as the patients who were submitted to surgery. Two of the three

had localized peritonitis. In the third case the process was spreading when the patient was first seen but was rapidly localized to the right lower quadrant (Fig 1). Treatment consisted of 0.5 Gm of streptomycin intramuscularly every four hours over a period of fourteen days. When interval appendectomy was performed six weeks after the original illness, there was no evidence of peritonitis.

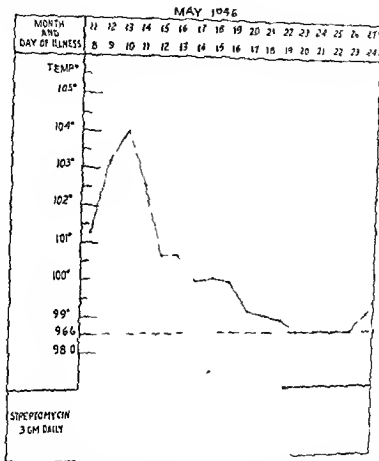
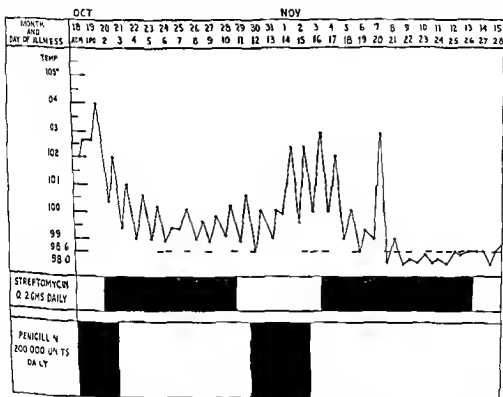


Fig 1—Localizing peritonitis of appendiceal origin. No operation was done. Regression of large mass in right lower quadrant could be followed from day to day.

Certain other cases are deserving of special mention. One patient who apparently had a localizing type of peritonitis was submitted to appendectomy and drainage of an abscess on the fifth day of illness. He had a very stormy postoperative course, characterized by recurring chills and temperature elevations to 106° F. The liver became enlarged and tender and he was slightly jaundiced. All the evidence pointed to a diagnosis of pyelophlebitis. Recovery with uncomplicated wound healing followed the administration of 2.5 Gm of streptomycin in divided doses daily for fourteen days supplemented by the usual supportive therapy. The drug was considered lifesaving in this case. In

two other cases however, in which streptomycin was used in conjunction with appendectomy and drainage of well localized appendical abscesses, it was thought that the uneventful recoveries were quite as likely to have ensued without adjuvant antibiotic therapy as with it

Four patients developed residual abscesses while one patient developed a pelvic abscess twenty eight days after drainage of an appendical abscess. In the interim combined penicillin and sulfadiazine therapy had been given with not particularly striking results. Parenteral streptomycin therapy was followed by prompt resolution of the abscess and prompt recovery without further surgery (Fig 2). Two patients with subhepatic abscesses and one with a



patients recovered in the face of myocardial disease, and a really dramatic response was obtained in another patient who was not operated upon.

Two of thirteen patients with localizing peritonitis (Table II) showed rapid improvement after the institution of therapy and did not require emergency operation (Fig 4). In six other cases the results were good although not remarkable. In two of the remaining cases the response was doubtful and

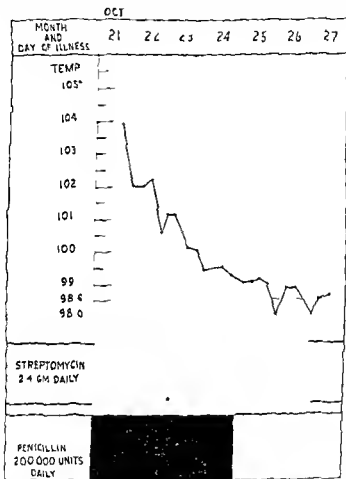


Fig 3—Localizing peritonitis of appendical origin. Recovery was rapid and uncomplicated after surgery.

in three cases there were no results at all. One patient in this group developed a pelvic abscess which required drainage on three occasions. In another case the stump of the appendix blew out but the resulting fecal fistula fortunately exteriorized and ultimately closed spontaneously. In still another case extension of the infection to the subphrenic space was suspected, but abscess formation did not follow.

PERITONITIS OF NONAPPENDICEM ORIGIN

Seven patients with peritonitis of nonappendiceal origin were treated only with streptomycin (Table I). There was one death from sepsis in a patient with multiple gunshot wounds. He was moribund when first seen, on the seventh day of illness and died within twenty-four hours. In two cases the results were excellent. One of these patients had been submitted to abdominal

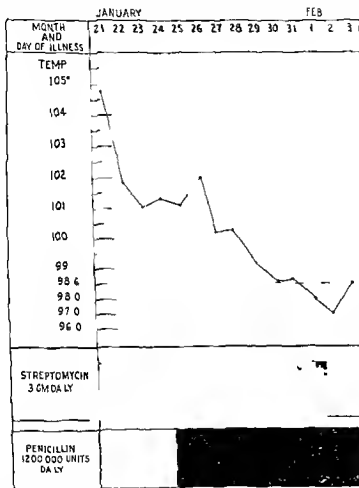


Fig 4—Localizing peritonitis of appendiceal origin. No operation was done. The fever was uncontrolled after three days of streptomycin therapy. The course was uncomplicated after penicillin was added to the regimen.

perineal resection. The other had carcinoma of the sigmoid which had ruptured into a loop of the ileum and then into the free peritoneal cavity. Drainage of the subsequent abscess yielded a thin pus without odor which grew only nonhemolytic streptococci. These organisms were moderately susceptible to streptomycin. Results in the two other cases in this group were doubtful in that improvement either was slow or followed the use of surgical drainage.

There were two deaths in seventeen patients with nonappendical peritonitis treated by streptomycin and penicillin with or without sulfadiazine (Table II). Both occurred in patients with stab wounds of the abdomen and both were due to vascular collapse and not to bacterial infection. In all cases of early spreading peritonitis the response was dramatic. The two patients who showed no improvement both had small doses of streptomycin, in one of these cases recovery was complicated by pulmonary atelectasis and pneumonia.

COMMENT

Of the five deaths which occurred in the sixty three cases of peritonitis presented in this communication, three were due to nonbacterial causes. In the other two cases, both of which were instances of generalized fibrinopurulent peritonitis, streptomycin was added to other therapy when the patients were already moribund apparently as a "panic" measure. Eighteen of the fifty eight patients who recovered were treated only with streptomycin, the remaining forty patients were treated with streptomycin and penicillin, supplemented in ten cases by sulfadiazine.

Immediate dramatic results were seldom observed following the administration of streptomycin, whether it was used alone or in combination with penicillin, although in both spreading and localized peritonitis recovery was thought to be smoother and more rapid when the drugs were used in combination. In no instance could any cumulative effect be attributed to the administration of streptomycin and sulfadiazine in combination.

Streptomycin was undoubtedly more effective in early spreading peritonitis although immediate dramatic results were not the rule whether it was used alone or with penicillin. Resolution of established peritoneal suppuration in the streptomycin series was of approximately the same pattern as is seen in patients receiving penicillin in excess of 800,000 units. While results were generally less striking when streptomycin was employed in infections which had already localized the impression was received that resolution occurred more rapidly in such cases when penicillin was also used. The combination gave particularly good results in three instances of pelvic inflammatory disease in which no demonstrable result had been achieved by penicillin therapy alone.

The dosage of streptomycin employed varied between 1 and 4 Gm. per day administered by the intramuscular route in divided doses at three or four hour intervals. In a few instances streptomycin in amounts up to 0.5 Gm. was introduced into the peritoneal cavity at the time of operation. There was no apparent adverse effect. The dosage of penicillin ranged between 120,000 and 600,000 units per day. The average dose of sulfadiazine was 6 Gm. daily.

Consistently beneficial effects could never be attributed to streptomycin when the dosage was 2 Gm. per day or less whether it was given alone with sulfadiazine or with penicillin in amounts of 240,000 units per day or less. No harmful effects were noted in consequence of daily dosages of 3 Gm. per day for ten to fourteen days although minor untoward reactions occurred in approximately 20 per cent of the cases. Patients who received 3 Gm. per day of streptomycin alone or 2.5 Gm. in combination with an average of 420,000 units of penicillin, had the most satisfactory postoperative convalescence. The re-

sponse to streptomycin therapy was practically always indifferent when adequate doses were used (15 Gm per day or less)

On the basis of this small series of cases it is impossible either to ascribe consistently beneficial effects to streptomycin therapy in peritonitis or to deny the possibility of therapeutic benefits in early established peritoneal suppuration. Clear cut beneficial results were generally more apparent in spreading than in localized processes.

SUMMARY AND CONCLUSIONS

1 Sixty three patients with peritonitis of various etiologies of whom five died received adjuvant streptomycin therapy alone or in combination with penicillin sulfadiazine was added in a few cases

2 The beneficial effects of streptomycin therapy in early spreading peritonitis closely paralleled those observed in cases in which large doses of penicillin were given. Streptomycin did not seem to be of particular value in localized peritoneal suppuration

3 On the basis of these preliminary studies it is apparent that streptomycin is not a panacea yet has a valuable place in the treatment of peritonitis. Used alone it is especially effective in spreading and in localizing types of infection without a palpable mass. Used in conjunction with penicillin it is effective in many patients who fail to respond to penicillin alone or to penicillin combined with sulfonamides

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STUDIES IN EXPERIMENTAL FROSTBITE

I THE EFFECT OF HEPARIN IN PREVENTING GANGRENE

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THE confusion which exists in the treatment of frostbite during the early phase is due largely to a difference of opinion regarding the chief mechanism by which permanent ischemic damage is produced. Some investigators have felt that the major difficulties are the result of reduced blood flow consequent to the swelling of the limb from edema and extravasation. They have directed treatment toward reducing the swelling and diminishing tissue metabolism by prolonging the period of thawing and by local cooling of the injured part. Others have felt, on the other hand, that the principal harm results from prolonged intense vasoconstriction and eventual thrombosis of arteries and arterioles. They have concentrated therapeutic efforts on elimination of vasospasm and prompt restoration of the best possible circulation. There is much to support this second concept.¹ An important additional means of treatment has been introduced recently by experiments suggesting that anticoagulants may be effective in preventing thrombosis and gangrene.

In 1944 Brambel and Loker² used dicumitol, sympathetic blocks and boric acid compresses to treat a patient in whom incipient bilateral gangrene of the toes had developed following frostbite. Some difficulty with bleeding from ulcerated areas occurred but healing took place with the loss of only the distal phalanx of one toe. Although it was conjecturable whether major amputation would otherwise have been required, they had the impression that anticoagulant therapy might have been responsible for the good result and suggested study of its usefulness in other cases of frostbite.

In 1945 Lange and Boyd³ reported experiments in frostbitten rabbits which were convincing of dramatic efficacy of heparinization in the prevention of gangrene. Subsequently Lange and Loewer⁴ reported that heparin was also brilliantly effective in preventing gangrene of skin in experimental contact frostbite in human volunteers. Since the present investigation was completed another report by Friedman, Lange and Womert⁵ has appeared confirming the usefulness of heparin in preventing gangrene following experimental frostbite in rabbits. Their investigation demonstrated that the chief pathologic changes following the initial vasoconstriction are vascular engorgement with conglutination of erythrocytes followed subsequently by true agglutinative thrombi, and that heparinization tends to prevent the formation of these thrombi.

These studies are of such importance in the pathology and treatment of frostbite that we believed it was worth while to carry out similar investigations. It was our desire to see whether the good results obtained by Lange and his co workers could be duplicated in another laboratory and with such uniformity as to justify the hopes which their reports naturally have raised. It was further hoped that more precise data could be accumulated concerning the relationship to the ultimate result of such factors as the degree of cold, the duration of exposure and the extent of the area frozen as well as the time of beginning treatment, the duration of treatment and its intensity. Unfortunately, the initial phases of this problem have proved so difficult that the project has not been completed. Since these studies have confirmed the fact that adequate heparinization is sometimes effective in preventing gangrene in experimental frostbite but have at the same time demonstrated that this treatment is by no means uniformly successful it is felt advisable to present our preliminary investigations. This is not done in order to discourage the use of anticoagulants in frostbite but rather to dispel any false sense of security which may prevail based upon the notion that such treatment may be regularly effective even in the severest cases.

MATERIALS AND METHODS

Domestic rabbits of mixed breed weighing from 2 to 3 kg were used. The hind limb to be frozen was carefully depilated at least twenty four hours before freezing in order to make sure that no significant injury to the skin had occurred. The rabbits were anesthetized for freezing with nembutal given intravenously. In a few experiments the limb was immersed directly in an ether dry ice mixture in the majority the limb was covered first with a rubber condom boot care being taken to prevent tearing of the boot or spilling over of the ether into it. In all instances constriction of the limb was studiously avoided. The degree of coldness of the solution varied as well as the duration of the exposure. In each freezing experiment it was noted whether or not actual freezing of the part had occurred and in the rare instances in which solid freezing did not take place the animal was discarded from the series. In all cases the limb was immersed up to the level of the hock. In most of the experiments the frozen limb was gently sponged with 1:1000 aqueous zephiran and covered with sulfathiazole ointment and sterile dressing applied snugly but in such a way as to cause no constriction. The dressings were changed occasionally but were continued until recovery was complete or gangrene was obviously well established. The details of each freezing experiment are recorded in the results.

Varying amounts of heparin in aqueous solution were administered intermittently by the intravenous route. Clotting time was determined upon some animals by the capillary tube method with blood obtained by puncture of the ear in others by the method of Lee and White⁸ with blood removed by cardiac aspiration.

RESULTS

This report is based upon observations of 66 rabbits, one hind limb of which was solidly frozen. Excluded are 2 rabbits in which the exposed limb did not become solidly frozen, 5 rabbits which died of unknown causes and 16 which died during the course of anticoagulant therapy before the outcome of the experiment could be determined. Of the 16 rabbits which died under heparin treatment the majority showed large retroperitoneal hemorrhage or other evidence of bleeding.

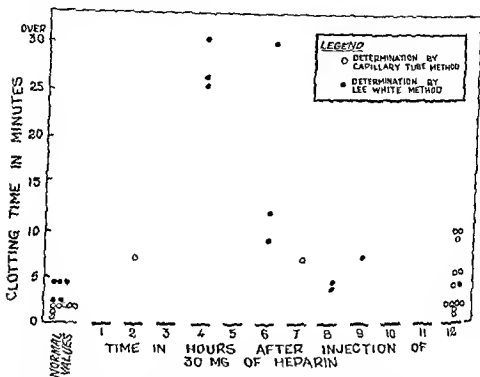


FIG. 1.—Clotting time values after single intravenous injection of 30 mg. heparin.

It was not found practicable to perform determinations of clotting time at frequent intervals during the course of treatment in order to be certain that in any given animal the prolongation of clotting time was constantly maintained during anticoagulant therapy. Not only is it impossible to remove blood by cardiac puncture at frequent intervals for a period of five or six days without causing death in a large number of animals but the removal of sufficient blood for the more reliable Lee White method during such a period would produce a severe anemia. Indeed it was found to be impracticable to secure blood for the capillary tube method five or six times daily by puncture of the ear since such efforts rapidly obliterated by local injury or extravasation the veins necessary for intravenous therapy. An effort to evaluate the

efficacy of varying doses of heparin had to be made by controlled experiments upon a number of animals rather than by routine determinations upon each one.

Since Lange and Boyd had given heparin every twelve hours intravenously in 30 mg doses, the effect of this treatment was first investigated. The results are recorded in Fig 1. With the capillary tube method, the values of normal control clotting time varied from 1 to 2 minutes, averaging 1.8 minutes. Twelve hours after injection of 30 mg of heparin the clotting time had returned to normal in one half of the animals; in the other one half it

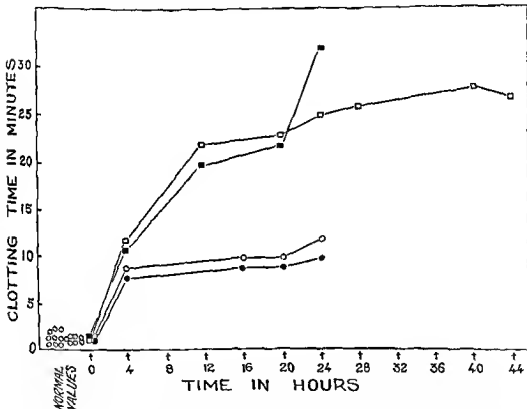


Fig 2.—Clotting time values during course of heparin treatment. The values designated by the open and by the shaded squares represent studies in two animals which were given 30 mg. of heparin intravenously at intervals of four hours; those represented by the open and shaded circles studies in two animals treated with 10 mg. of heparin intravenously at intervals of four hours. Blood for clotting time determination was drawn in each instance immediately before heparin was administered.

ranged from 4 to 10 minutes. The control coagulation time values with the Lee White method ranged from 2.5 to 1.5 minutes, averaging 3.7. The clotting time was well prolonged four hours after injection of heparin but became less prolonged thereafter, and in 3 of 4 animals was within the normal range from eight to twelve hours after injection. The conclusion was reached that one could not rely upon 30 mg. of heparin given every twelve hours to provide constant prolongation of coagulation time.

In Fig 2 data are recorded showing that 10 mg of heparin given intravenously every four hours keeps the clotting time not less than from 8 to 12 minutes, and that 20 mg of heparin given in similar fashion maintains the clotting time between 20 and 30 minutes. A few additional studies confirmed the observations from the 4 experiments which form the basis for this chart. It will be noted that the normal control values with the Lee White method were different in the two sets of experiments recorded in Figs 1 and 2, these sets of experiments were carried out by different investigators. Although the results of this determination vary somewhat with different observers, they are reasonably reliable in the hands of one observer.

The initial experiments are recorded in Table I and represent an effort to determine whether gangrene following severe degrees of direct contact freezing can be prevented by small or large amounts of heparin. The depilated hind limb of the anesthetized rabbit was immersed without protection of a rubber boot up to the hock in an ether carbon dioxide snow mixture at from -20° to -40° C. No dressings were placed upon the frozen limb. Extensive gangrene developed in all animals whether the limb was frozen 5, 20, 30, 50, or 90 minutes. Four animals were given a single 30 mg injection of heparin 30 minutes after freezing for one half hour, and one was treated at four hour intervals for sixty four hours with the same dose. Two animals which were subjected to freezing of a foot for one hour were treated at four hour intervals with 20 mg of heparin for a forty eight hour period, 2 others for a ninety six hour period and 2 others for 144 hours. One rabbit one foot of which was frozen for 90 minutes received 30 mg of heparin every twelve hours for

TABLE I RESULTS OF EXPOSURE OF THE DEPILATED UNPROTECTED FOOT OF RABBITS TO ETHER CARBON DIOXIDE SNOW MIXTURE AT FROM -20° TO -40° C, WITH AND WITHOUT HEPARIN THERAPY, NO DRESSING APPLIED TO FROZEN LIMB

TREATMENT	NO OF ANIMALS	RESULT	
		GANGRENE OF ENTIRE APLA FROZEN (NO OF ANIMALS)	GANGRENE NEARLY TO UPPER LIMIT OF AREA FROZEN (NO OF ANIMALS)
Exposure 5 minutes			
None	1	1	
Exposure 20 minutes			
None	1	2	
Exposure 30 minutes			
None	1	1	
30 mg heparin 30 min after freezing	4	4	
Same continued q 4 hr to 64 hr	1	1	
Exposure 60 minutes			
20 mg heparin 30 min after freezing and q 4 hr for 48 hr	-	-	1
Same for 96 hr	-	-	2
Same for 144 hr	-	-	
Exposure 90 minutes			
None	1	1	
30 mg heparin q 12 hr for 48 hr	1	1	

forty eight hours. The extent and character of the gangrene were precisely the same in the treated and untreated animals with the exception of the 2 rabbits treated with heparin at four hour intervals for six days, in these two complete dry gangrene extended almost but not quite up to the upper level of the frozen area.

The second set of experiments are recorded in Table II. The depilated hind limb of the anesthetized rabbit was covered with a rubber condom boot and was immersed up to the hock for varying periods in ether maintained at a temperature of from -12° to -20° C. By placing a beaker filled with ether inside a larger container filled with ether and dry ice and by stirring the fluid in the beaker and constantly checking its temperature with a thermom-

TABLE II. RESULTS OF EXPOSURE OF DEPILATED FOOT OF RABBIT PROTECTED BY CONDOM BOOT, IN ETHER KEPT AT FROM -12° TO -20° C, WITH AND WITHOUT HEPARIN THERAPY

TREATMENT				RESULT				
AMT HEPARIN AND FREQUENCY OF INJECTION	TIME AFTER FREEZ- ING PX BEGUN	DURA- TION OF RX (IN HR)	NO OF ANI- MALS	NO GANG- RENE OR ULCER (NO OF ANIMALS)	SUPET- FICIAL ULCER ONLY (NO OF ANIMALS)	GANG- RENE LIMITED TO TOES (NO OF ANI- MALS)	GANGRENE COMPLETE UP TO WITHIN 1 TO 2 CM OF UPPER 1/2 OF FREEZING (NO OF ANIMALS)	GANG- RENE OF ENTIRE FOOT (NO OF ANIMALS)
Exposure 10 minutes								
None			3					3
10 mg q 4 hr	30 min	24	1					1
10 mg q 4 hr	90 min	48	1					1
10 mg q 4 hr	30 min	96	1					1
10 mg q 4 hr	90 min	120	1					1
20 mg q 4 hr	30 min	48	1					1
20 mg q 4 hr	90 min	96	2				1	1
20 mg q 4 hr	90 min	144	2					2
30 mg q 4 hr	0 min	48	1			1		
30 mg q 4 hr	30 min	96	1		1			
30 mg q 4 hr	90 min	120	1		1			
Exposure 45 minutes								
30 mg q 12 hr	0 min	72	2					2
Exposure 30 minutes								
None			7					7
20 mg q 4 hr	30 min	72	1					1
20 mg q 4 hr	0 min	96	1					1
20 mg q 4 hr	30 min	120	1				1	1
20 mg q 4 hr	30 min	144						3
20 mg q 4 hr	2 hr	144	2			2		
20 mg q 4 hr	4 hr	144	1				1	
20 mg q 4 hr	10 hr	144	1				1	
30 mg q 4 hr	90 min	64	1	1				
30 mg q 4 hr	90 min	140	1					1
Exposure 15 minutes								
None			2					2
Exposure 10 minutes								
None			4					4
20 mg q 4 hr	30 min	48	2		1	1		
20 mg q 4 hr	30 min	144	7	2	1			4
20 mg q 4 hr	10 hr	144	1					1
Exposure 5 minutes								
None			1		1			

eter which was left in place and by adding dry ice as needed to the outside mixture it was not difficult to regulate the temperature. The frozen foot was kept entirely dry. Immediately after freezing the limb was sponged with zephiran and covered with sulfathiazole ointment and sterile dressings.

Fifteen limbs were frozen for 60 minutes. The control animals had complete gangrene up to the upper level of freezing. Four were treated with 10 mg of heparin every four hours for varying periods, 5 with 20 mg and 3 with 30 mg. All save 4 had gangrene as extensive as that of the controls. In one rabbit treated for four days with 20 mg doses complete gangrene appeared but not quite up to the hock. One animal treated for forty eight hours with 30 mg doses had gangrene limited to the toes whereas in 2 treated for 96 and 120 hours there were only small superficial ulcers and no deep gangrene.

In 13 animals the foot was frozen for 30 minutes. The 7 controls had complete gangrene of the entire frozen area. Two rabbits were given 30 mg doses of heparin for 64 and 120 hour periods; in the first there was no gangrene but the second had gangrene of the entire foot. Five of the 10 rabbits treated with 20 mg doses of heparin showed gangrene of the entire foot. In 3 the gangrene was of slightly less extent and in 2 it was limited to the toes.

One foot each of 14 rabbits was placed in the freezing solution for only a 10 minute period. In the 4 control animals the gangrene was complete but involved an area extending only up to within 1 to 2 cm of the upper level of freezing. One of the 2 rabbits treated for two days had gangrene only of some of the toes and the other had only a superficial ulcer. In 4 of the 7 rabbits treated for a six day period however there was as extensive gangrene as in the controls. In 2 no gangrene appeared; in the third there was only a superficial ulcer. Gangrene was complete in the one rabbit treated for six days in which treatment was begun ten hours after freezing.

In those rabbits in which gangrene was averted there was sensory loss in the foot during the period of observation which in general covered two weeks. In 3 rabbits the blood flow to one foot was completely occluded for 30 minutes and in 3 others for one hour by a rubber tourniquet tightly applied about the leg. None of these animals had gangrene or motor or sensory disturbance.

DISCUSSION

The first experiments recorded failed to demonstrate that small or larger amounts of heparin were effective in preventing gangrene when the unprotected foot was frozen for rather long periods in a mixture kept at from -20° to -40° C. These experiments are of limited significance since there were few animals which were adequately heparinized for a prolonged period.

The second set of experiments deal with the treatment of frostbite of less extent than that treated by Lange and his co-workers. Lange and Boyd reported that of 11 anesthetized rabbits the deplated hind limb of each of which was frozen up to the knee for from 45 to 90 minutes in a solution kept at from -12° to -20° C. 2 died of hemorrhage and 2 showed superficial necrosis of considerable extent but these and the 7 other survivors recovered without loss of tissue.

Friedman Lange and Weiner have recently reported that there was no other evidence of gangrene than occasional small areas of focal necrosis in 13 rabbits in which the clotting time never fell below 30 minutes during treatment after freezing of a hind limb up to the knee for one half hour in a mixture kept at -30°C and in 4 of the 7 rabbits similarly prepared and treated in which the clotting time was not kept constantly so prolonged. These animals were sacrificed from two to nine days after freezing.

In the experiments which we have recorded the limb was similarly protected with a rubber boot cleansed with a mild antiseptic solution and dressed with sterile bandage after freezing. The area of limb exposed was less being only up to the level of the hock rather than up to the knee. The time of exposure was reduced to as little as 10 minutes. Although Lange and Boyd give no detailed information in regard to heparin therapy they imply that it was the same as they used in experiments in direct spot contact freezing in which they gave 30 mg of heparin intravenously every twelve hours for a period of at least five days beginning treatment from one half to three hours after freezing ended. In the experiments of Friedman Lange and Weiner heparin was given in 50 mg doses at twelve hour intervals. In some of our experiments the same daily dose of 60 mg of heparin which Lange and Boyd used was given but in a manner which provides more constant prolongation of clotting time namely by administration at intervals of four hours. In other experiments 20 and 30 mg of heparin were given every four hours. Control studies demonstrated constant prolongation of clotting time when 10 mg of heparin was given at four hour intervals and greater prolongation when 20 mg doses were used. Many of the animals in which 30 mg of heparin were given at four hour intervals and some of those similarly treated with 20 mg doses died of hemorrhage before completion of the experiment.

It is difficult to explain why in our experiments with exposure of a smaller area for a shorter interval of time and with a more efficient method of anticoagulant therapy the results were so inferior to those reported by Lange and his associates. If we consider only those animals which were treated for five days or more it is seen that deep gangrene was prevented in only 4 of 21 rabbits treated in incidence of 19 per cent. If 3 animals are eliminated in which treatment was started after an interval of more than three hours after completion of freezing 4 of 17 animals or 23.5 per cent escaped deep gangrene. Two additional animals had gangrene limited to the toes. If they are included 6 of 17 or 35.3 per cent escaped disabling permanent loss of tissue. This fact is in contrast to the protection against deep gangrene in all of the small group treated by Lange and Boyd in all of the 13 rabbits treated by Friedman Lange and Weiner in which the clotting time did not fall below 30 minutes and in 4 of 7 in which the clotting time was occasionally less.

There can be no doubt that in certain animals heparin therapy was responsible for preventing gangrene or lessening its extent. It will be noted that every untreated animal the foot of which was frozen during an exposure of 30 minutes or longer had complete gangrene up to the level of freezing and that in untreated animals gangrene of only slightly less extent invariably

followed an exposure of 10 or 15 minutes. The 11 animals in which gangrene was averted or was limited to the toes or to superficial ulceration were all treated with heparin as were the 4 rabbits exposed for 30 minutes or longer in which the gangrene, though extensive did not include the proximal 1 or 2 cm of the area frozen.

Unfortunately our experiments do not permit we feel clear cut conclusions concerning certain important related problems. It is not clear from the data recorded in Table II for example that when four hour heparin therapy begun within two hours of the termination of freezing was continued for five days or more, the results were better than when treatment was kept up for a shorter period. Six of the 17 rabbits (35.3 per cent) which were so treated for five days or more had no gangrene or only superficial ulceration or loss of toes whereas 5 of 13 (38.5 per cent) treated for shorter periods recovered with similarly slight loss of tissue. On more careful analysis the results are seen to be rather contradictory. In the case of those animals in which the exposure was 10 minutes and in which treatment with 20 mg of heparin was begun promptly and continued at four hour intervals for forty eight hours only minor loss of tissue occurred whereas this was true in only 3 of 7 rabbits treated similarly for six days. On the other hand minor loss of tissue took place in 2 of 5 rabbits exposed for 30 minutes and treated promptly with heparin and for a period of five or six days whereas both of the rabbits similarly exposed but treated with the same dose for shorter periods had complete gangrene of the foot.

It is of interest that 5 of 9 rabbits exposed for 10 minutes and treated promptly with heparin in 20 mg doses given at four hour intervals had no gangrene or had only slight loss of tissue (55.6 per cent) whereas such good results prevailed in only 2 of 8 rabbits (25 per cent) similarly treated after a 30 minute exposure and in none of 5 treated in the same manner after a 60 minute exposure. In 1 of 2 rabbits a foot of which was exposed for 30 minutes treated promptly with heparin given in 30 mg doses at four hour intervals no gangrene developed and in all 3 similarly treated after a 60 minute exposure there were only superficial ulcers or gangrene limited to the toes. In contrast all 4 rabbits treated with 10 mg doses after a 60 minute exposure had complete gangrene of the foot. The 5 rabbits treated with heparin given at intervals of twelve hours or at more frequent intervals but after a delay before onset of treatment of from four to ten hours following freezing had extensive gangrene although in 2 it was slightly less extensive than that observed in the controls. Five of 9 treated rabbits (55.6 per cent) had only minor loss of tissue or no gangrene at all in the group exposed for 10 minutes 3 of 12 (25 per cent) exposed for 30 minutes and 3 of 12 (25 per cent) exposed for 60 minutes. The last group includes some animals treated only with 10 mg doses of heparin but it also includes some treated with 30 mg doses which were used in only a few of the second group and in none of the first.

These observations suggest that the milder the frostbite the more efficacious heparin therapy may be expected to be and vice versa and that the more prolonged the coagulation time the greater the efficacy of anticoagulant

therapy in preventing gangrene. They suggest also that such treatment may be futile unless it is begun promptly after freezing. They demonstrate conclusively two facts: first, that heparin therapy is of some efficacy in preventing or limiting in extent and degree the gangrene of experimental frostbite, and second that this therapy is not as uniformly successful as has been reported by others.

The careful pathologic studies of Friedman, Lange, and Weiner failed to demonstrate any significant nerve damage in frostbitten rabbits adequately treated with heparin. In the experiments of Lange and Boyd and in our own sensory loss followed frostbite even when gangrene was averted by use of anticoagulant therapy. In contrast when the circulation to the foot was completely shut off by tourniquet for periods equal to or greater than those of the exposure, no sensory loss followed. This would suggest that cold itself may bring about at least a functional alteration of the nerves.

The studies reported confirm the plausibility of the important suggestions of Brambel and Loker and of Lange and his co-workers that the use of anticoagulant therapy should be investigated in clinical cases of injury due to cold and that this therapy may be expected to be a valuable aid in the management of such problems. They would lead one to believe that this treatment cannot be expected to avert gangrene in every instance. It should be pointed out to be sure that frostbite in man is often less severe than that utilized in this experimental study. On the other hand patients with frostbite are often not available for treatment as soon after injury as was practiced in our investigation. Furthermore heparin cannot be given to man in near fatal amounts as we have done in our experiments. The ultimate usefulness of anticoagulant therapy in human injuries due to cold must await clinical trial. Because in animal experimentation alone the various related factors can be adequately controlled however it may be anticipated that many important observations concerning the problem of anticoagulants in frostbite will necessarily depend upon such investigations.

CONCLUSIONS

Adequate heparinization is a valuable but not an invariably reliable therapeutic aid in the prevention or limitation in extent and degree of gangrene in experimental frostbite in rabbits.

The authors wish to express their appreciation to Mr. Joseph A. Arena for his assistance.

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THE USE OF ANTICOAGULANTS IN THE SURGERY OF ANEURYSMS AND ARTERIOVENOUS FISTULAS, WITH PARTICULAR REFERENCE TO DICUMAROL

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DURING the recent war an opportunity at one of the Vascular Centers was afforded us to study the clinical applicability of anticoagulant therapy in vascular surgery. The clinical material consisted of a group of patients in whom some type of reparative or restorative procedure had been employed in an effort to maintain the continuity of the affected artery following surgical obliteration of a peripheral aneurysm or arteriovenous fistula. Heparin and dicumarol were used either alone or together.

Since the reported experimental and clinical data regarding anticoagulant therapy in arterial surgery are limited to the use of heparin alone,^{1,2} it was felt advisable to present our experiences. Furthermore, it was hoped that it would be helpful to record the methods and means of control of the therapy employed to discuss the general results and complications encountered, and to demonstrate that reparative surgery of the peripheral arteries can be safely accomplished with anticoagulants given at the time of operation or before. The material was insufficiently controlled, however, to warrant drawing definite conclusions concerning the efficacy of anticoagulants in the prevention of thrombosis following arterial repair.

CLINICAL MATERIAL AND METHODS

Some type of reparative procedure was performed in 34 of 290 aneurysms and arteriovenous fistulas treated surgically,³ and of this number 22 patients were given anticoagulant therapy for a more or less prolonged period of time. An additional patient received a single injection of heparin. The basis for the selection of cases for repair and the clinical results have been presented elsewhere.⁴ The methods employed for preserving the continuity of the vessel consisted of ligation and transfixion of the fistula, lateral arteriorrhaphy, resection of a segment of artery with end to end suture, and vein transplantation. Anticoagulant therapy was used infrequently with the first method, generally with the second, and routinely with the other two (Table I).

Crystalline heparin in aqueous solution was administered every four hours by the intravenous route, in 50 mg. doses. The first injection was given at the time of operation as soon as the decision was made to attempt arterial repair. In general, it was utilized only during the initial period of dicumarol therapy until a satisfactory alteration of prothrombin level had been obtained with

TABLE I RESULTS IN CASE OF AETHEUM REPAIR

TYPE OF REPAIR	NO. OF CASES	NO. RECEIVING ANTICOAGULANTS	NO. OF CASES IN WHICH THROMBOSIS OCCURRED
transection of fistula	13	4 [*]	0
Lateral arteriorrhaphy	5	3	1
End-to-end suture	10	10	2
Vein transplantation	6	6	1

*One of these patients received only a single 50 mg. dose of heparin.

the latter. The anticoagulant effect was measured occasionally but not regularly by clotting time determinations carried out according to the method of Lee and White.⁴

Dicumarol was administered to any given patient only after an initial prothrombin level had been obtained. In general, 300 mg. were given the first day, 200 mg. the second day, and 100 mg. on the third day. Thereafter the dosage was determined on the basis of the level of the daily prothrombin time. The exact quantity required to maintain the prothrombin time at the desired level varied for the different patients and not infrequently for the same patient during the course of therapy. Generally a daily dose of 100 mg. was necessary, although in some instances smaller amounts were adequate. When patients were being given heparin and dicumarol concurrently, blood for prothrombin determinations was drawn just before the administration of a dose of heparin in order to minimize any possible effect of the latter upon the prothrombin blood level determination. It was found to be a safeguard to delegate the dicumarol therapy to one member of the staff who received a report of the prothrombin determinations each morning and then gave necessary orders with regard to dosage. An effort was made to maintain the prothrombin level around 20 to 30 per cent of normal according to the Quick curve⁵; this is roughly equivalent to a "clotting index" of 50.

The method of Quick⁵ was used for the determination of prothrombin time. Four and one half cubic centimeters of blood were withdrawn by venopuncture and placed in a test tube containing 0.5 c.c. of 13 per cent sodium oxalate. The contents of the tube were well mixed and then centrifuged. Three Loeffler test tubes into each of which 0.1 c.c. of the plasma was introduced, were placed in a water bath kept at from 35° to 40° C. One tenth cubic centimeter of thromboplastin,* previously brought to the same temperature was added to each tube being blown from a pipette so as to bring about immediate mixing. One tenth cubic centimeter of calcium chloride was then quickly blown from a pipette into each of the test tubes and simultaneously a stop watch was started. After a short interval one of the tubes was removed from the bath held up against a light, and tilted back and forth until clotting took place, the end point was considered to be the time at which the particles of thromboplastin ceased moving while the plasma continued to do so. Care was taken to avoid marked agitation of the contents of the tube. The watch was stopped and read at the moment clotting was noted. Two of the test tubes were used for preliminary guide

*The thromboplastin was obtained as Bacto Thromboplastin from the Difco Laboratories Incorporated, Detroit, Mich., or was prepared in the laboratory from rabbit brain.

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by
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TABLE II CASES IN WHICH THROMBOSIS OCCURRED

CASE NO	TYPE AND LOCATION OF LESION	TYPE OF REPAIR	ANTICOAGULANT THERAPY	PROBABLE CAUSE OF THROMBOSIS
1	Femoral AA fistula	Lateral anterior rhaphy	None	Local damage to artery operative constriction of lumen
2	Brachial aneurysm	End to end suture	Heparin* dicumarol 2	Local damage of artery
3	Brachial aneurysm	End to end suture	Heparin 2 hrs dicumarol 2 weeks	Local damage of artery
4	Brachial aneurysm	Vein graft	Heparin 50 mg dicumarol 2 weeks	Questionably imperfect suture due to small caliber of lumen

*Through error this patient received 400 mg of heparin and 1500 mg of dicumarol during the first seventeen hours after operation. Anticoagulants were stopped at this time and 60 mg of synthetic vitamin K were given.

heparin was administered immediately after operation and dicumarol was continued for two weeks. The other was one referred to previously in whom a very large amount of dicumarol was given erroneously during the first twenty hours postoperatively after which all anticoagulant therapy was discontinued. In both thrombosis could reasonably have been attributed to the local arterial damage. The third patient was one in whom a brachial aneurysm was excised and a vein graft was performed. An adequate prothrombin level had already been achieved with dicumarol at the time of operation. A single dose of heparin was given during the surgical procedure and dicumarol was continued for about two weeks. No explanation for the cause of thrombosis is evident although it is not unlikely that an imperfect suture may have been performed because of the unusually small size of the artery even though the completed anastomosis appeared satisfactory at the time of operation. It is important to point out that there was no evidence of propagation of a clot in any of the 3 cases in which thrombosis of the repaired segment occurred.

In no case in the series of patients receiving anticoagulants was any particular difficulty with hemostasis experienced at operation regardless of whether heparin was given immediately before the anastomosis was accomplished or whether the prothrombin time had been altered beforehand through the administration of dicumarol. As a safeguard fibrin foam was often placed in the wound a precaution which appeared to give some protection against bleeding from the operative site without adding any risk of intravascular clotting.

In several cases some later difficulties with bleeding were encountered. One patient who had a lateral suture of the subclavian artery and who was receiving dicumarol developed a hematoma of moderate size in the wound. The operative site was explored on the tenth day and a clot was evacuated. No bleeding was encountered and the wound was closed. Convalescence was uneventful. Another patient upon whom a vein graft to the popliteal artery had been performed had a small hematoma which was evacuated without difficulty in bed. He had no further bleeding during the six weeks period in which dicumarol was administered. A third patient had developed a large hematoma

readings and the third for more precise determination of the clotting time. A control test with normal plasma was run with each daily set of determinations. Values were expressed in per cent of normal utilizing the curve developed by Quick.⁴

RESULTS

The method of administration of anticoagulants varied in the different cases. In 18 patients combined heparin and dicumarol therapy was utilized. The operative procedure carried out in this group consisted of ligation and transfixion of the fistula in 1 instance, lateral arteriorrhaphy in 3, end-to-end suture in 10, and vein transplantation in 4. The heparin was begun at the time of operation and administered in 50 mg. doses at four hour intervals for an average of two days. The dicumarol was started as soon after operation as a prothrombin determination could be obtained and in most instances it was continued for a period of three weeks. In a few cases it was given only for a period of from ten to sixteen days while in 4 it was used for an even shorter period of time. In one of the latter it was discontinued after six days because of an unusually marked response resulting in a very low prothrombin level. In another in whom a lateral suture had been performed in the presence of gross infection dicumarol was stopped after the third day while in the third it was not given after the fourth day because of persistent bleeding from the wound.

The fourth case in the group receiving dicumarol for a short period of time deserves more detailed presentation. In this instance in which a brachial aneurysm was excised and an end-to-end suture accomplished heparin was started at the time of operation and dicumarol was administered shortly afterward. Through an error the patient received 300 mg. of dicumarol every four hours for five doses in addition to 50 mg. of heparin every four hours during the same period of time. When the mistake was recognized all anticoagulant therapy was stopped and 60 mg. of synthetic vitamin K were administered intravenously. The prothrombin level remained fairly low for several days but not alarmingly so and no hemorrhagic difficulties ensued.

In four cases dicumarol was given before and an adequate reduction in prothrombin level had already been attained at the time of surgery. Two of these patients in whom vein transplantation was performed also received a single dose of heparin during the operation while in the other two in whom a fistula was transfixed and the vein divided no anticoagulant other than dicumarol was utilized. In all four dicumarol was continued for a period of approximately three weeks. The last patient in the series received no anticoagulant treatment other than a single dose of heparin given at the time of operation.

Three patients developed thrombosis despite the use of anticoagulants (Table II). In two of these a traumatic aneurysm of the distal end of the brachial artery existed and in both it was possible to resect the aneurysm and perform an end-to-end suture. The proximal end of the artery sutured was perfectly normal but in each instance the distal portion was somewhat scarred. However, further resection back to more normal appearing vessel wall was prohibited by the proximity of the point of bifurcation. In one of these patients

TABLE II CASES IN WHICH THROMBOSIS OCCURRED

CASE NO	TYPE AND LOCATION OF LESION	TYPE OF REPAIR	ANTH COAGULANT THERAPY	PROBABLE CAUSE OF THROMBOSIS
1	Femoral A-A fistula	Lateral arterial anastomosis	None	Local damage to artery operative constriction of lumen
2	Brachial aneurysm	End to end suture	Heparin + dicumarol	Local damage of artery
3	Brachial aneurysm	End to end suture	Heparin 50 mg daily for 2 weeks	Local damage of artery
4	Brachial aneurysm	Vein graft	Heparin 50 mg daily for 2 weeks	Questionably imperfect suture due to small caliber of lumen

*Through error this patient received 100 mg of heparin and 1500 mg of dicumarol during the first seventeen hours after operation. Anticoagulants were stopped at this time and 60 mg of synthetic vitamin K were given.

heparin was administered immediately after operation and dicumarol was continued for two weeks. The other was one referred to previously in whom a very large amount of dicumarol was given erroneously during the first twenty hours postoperatively after which all anticoagulant therapy was discontinued. In both thrombosis could reasonably have been attributed to the local arterial damage. The third patient was one in whom a brachial aneurysm was excised and a vein graft was performed. An adequate prothrombin level had already been achieved with dicumarol at the time of operation. A single dose of heparin was given during the surgical procedure and dicumarol was continued for about two weeks. No explanation for the cause of thrombosis is evident although it is not unlikely that an imperfect suture may have been performed because of the unusually small size of the artery even though the completed anastomosis appeared satisfactory at the time of operation. It is important to point out that there was no evidence of propagation of a clot in any of the 3 cases in which thrombosis of the repaired segment occurred.

In no case in the series of patients receiving anticoagulants was any particular difficulty with hemostasis experienced at operation regardless of whether heparin was given immediately before the anastomosis was accomplished or whether the prothrombin time had been altered beforehand through the administration of dicumarol. As a safeguard fibrin foam was often placed in the wound a precaution which appeared to give some protection against bleeding from the operative site without adding any risk of intravascular clotting.

In several cases some later difficulties with bleeding were encountered. One patient who had a lateral suture of the subclavian artery and who was receiving dicumarol developed a hematoma of moderate size in the wound. The operative site was explored on the tenth day and a clot was evacuated. No bleeding was encountered and the wound was closed. Convalescence was uneventful. Another patient upon whom a vein graft to the popliteal artery had been performed had a small hematoma which was evacuated without difficulty in bed. He had no further bleeding during the six weeks period in which dicumarol was administered. A third patient had developed a large hematoma

shortly after excision of a femoral arteriovenous fistula and vein transplantation. The wound was reexplored two hours after operation and brisk bleeding from a small muscle branch was found. This artery was ligated, the wound was closed and no further difficulty ensued although dicumarol was continued for several weeks.

In a fourth patient a slow, steady oozing of bright blood from the wound was noted shortly after a femoral arteriovenous fistula had been excised and a vein graft performed. In spite of this bleeding heparin was continued intermittently until an adequate prothrombin level had been obtained with dicumarol. On the fourth day the dicumarol was stopped since by this time blood loss had been sufficient to result in a significantly lowered erythrocyte count. The patient was given 50 mg of synthetic vitamin K and a transfusion of whole blood and the wound was explored. Only diffuse capillary bleeding was found, the wound was closed and no further bleeding took place. In none of these patients did thrombosis of the repaired segment take place.

In another instance the brachial artery remained patent after lateral anastomosis in the presence of gross infection. However hemorrhage occurred through the unhealed suture line on the thirteenth postoperative day and as a result excision of the segment had to be carried out. Since dicumarol had been discontinued ten days before the bleeding took place it seems unlikely that this agent was implicated in the untoward response but rather that it was due to the nonhealing consequent to the infection.

It is of interest to discuss some of the findings in the 11 of the 34 patients in the series in whom anticoagulant therapy was not utilized. In one a femoral arteriovenous fistula was resected and the rent in the artery was repaired by a lateral suture. There was obvious injury to the artery wall in the neighborhood of the fistula and the vessel was constricted to about one half of its diameter by the suture. It appeared doubtful that the procedure would be successful at the time of operation but it was decided to do nothing further since blood flowed freely through the segment. Two hours after operation it was apparent from the absence of pulses in the popliteal, dorsal pedal and posterior tibial arteries that thrombosis had occurred. The wound was reexplored and a thrombus was found sharply limited to the repaired segment of the artery and without proximal or distal propagation. It was excised and the artery was ligated. In retrospect it would seem that the segment should have been excised originally and a vein transplantation performed. It also would have been wise to have used anticoagulants.

In another patient in whom a fistula was ligated and transfixed the only instance in which this procedure was not supplemented by division of the vein and use of the cuff of vein for buttressing, the healed fistula a prompt recurrence took place. This necessitated subsequent excision and quadruple ligation of the vessels. In the remaining 9 patients in this group thrombosis did not occur and no other untoward results were observed.

Of the series as a whole in 28 cases the arterial reparative procedure was entirely successful since the patency of the repaired segment was subsequently

evident from various observations and tests. In the remaining 6 instances described previously, in which the results locally were not satisfactory, no gross impairment of circulation to the extremity followed.

DISCUSSION

The clinical applicability of anticoagulant therapy in operative cases is being more precisely defined as a broader experience is being obtained. It is becoming evident that the desired anticoagulant effect is hazardous during certain operations within the abdomen, thorax, and cranial cavity, where postoperative bleeding may be unrecognized until the patient's life is in jeopardy and where control of hemorrhage is difficult. In such cases it is necessary to delay the use of anticoagulants until sometime postoperatively and then only in cases in which it can be reliably assumed that all bleeding has ceased. Certain operations upon bones and joints fall into the same category. On the other hand the present report demonstrates that surgery of the peripheral arteries can be undertaken at a time when a full anticoagulant effect has already been obtained either from dicumarol or heparin. One must be sure, however, that adequate hemostasis has been achieved before the wound is closed. Fibrin foam seems to be helpful in regard to control of capillary bleeding and undoubtedly certain other coagulant sponges would be similarly useful. Despite such precautions it appears reasonable to assume that the use of anticoagulants will result in an increase in the incidence of hematoma and in persistent oozing of wounds. Nevertheless the possible dangers of such complications are minimal if they are recognized promptly and are treated properly by surgery if indicated by cessation of anticoagulant therapy, and by the use of reversing agents such as synthetic vitamin K.

The efficacy of heparin in preventing thrombosis in cases of arterial repair is suggested both by experimental and by clinical observations.^{1,2} That dicumarol is of benefit in reducing the incidence of postoperative venous thrombosis and pulmonary embolism is also indicated by the good results which have been obtained by us and by others in clinical cases.^{3,4} On the basis of such experiences, it would seem likely that dicumarol should also be effective in reducing the incidence of thrombosis after arterial repair. However, the present report does not furnish complete proof of such efficiency, since no comparable group of patients was treated without anticoagulants and since most of our patients received heparin as well as dicumarol. The 11 cases in the series in which this therapy was not utilized cannot serve as proper controls, since most of them are patients upon whom the simpler types of reparative surgery were performed while anticoagulants were generally reserved for those in whom the type of repair was such that the hazard of thrombosis was greater. Nor can untreated cases from the literature be used for this purpose since so many other factors are important in the success of arterial surgery as, for example, the type of repair, the proficiency of the operator, the presence or absence of infection and the degree and extent of the local arterial injury or disease. It is our impression, nevertheless, that dicumarol and heparin were of benefit in preventing arterial thrombosis in the present series. That they are not

a complete safeguard is suggested by the finding that an adequate and prolonged anticoagulant effect did not prevent thrombosis in two of our patients. It appears evident that, helpful as anticoagulants may be, they will not assure success, unless the local damage to the sutured artery is not great and unless the surgical repair is properly performed.

It is of interest that in none of the 4 cases of thrombosis was there evidence of extension of the clot from the repaired segment. That the maintenance of good blood flow in the distal segment through adequate collateral channels is important in this regard is evidenced by the fact that there was no propagation of thrombus in the one instance in which anticoagulants were not used as well as in the 3 in which they were. Nevertheless, it is reasonable to assume that anticoagulant therapy will also prove of aid in this important problem of prevention of distal extension of the clot.

Up to this point we have discussed the use of anticoagulants only in those cases in which some reparative procedure was carried out. It is appropriate to inquire into its possible usefulness in patients in whom the affected artery is not repaired but is ligated and divided. We did not use anticoagulants in this series and only in 2 of the 256 cases³ did postoperative thrombosis occur. A nonfatal partial hemiplegia presumably due to distal propagation of thrombus developed in one patient some hours following ligation of the internal carotid artery for an intracranial carotid aneurysm. In the other instance a disaster of such moment took place that it appears of interest to present a detailed account of the occurrence.

The patient had a femoral arteriovenous fistula just distal to the point at which the profunda was given off which necessitated excision and quadruple ligation of the vessels. The foot maintained good circulation until the sixth postoperative day when the patient suddenly developed intense pain in the calf and foot followed by swelling of the leg and coldness, pallor and numbness of the foot. On examination it was evident that extensive venous and arterial thrombosis had occurred. In spite of a poor temperature and color response to spinal anesthesia, sympathectomy was performed as a last resort. The warmth and sensation of the foot were actually improved significantly by this procedure, although the increase in circulation was insufficient to prevent gangrene of the sole of the foot subsequently necessitating amputation. Anticoagulants were begun shortly after the difficulty was first noted without any apparent therapeutic effect.

Although this is the only case in a large experience in which postoperative thrombosis occurred in an extremity it makes one wonder whether the routine use of anticoagulants in the surgery of peripheral aneurysms and fistulas might disastrous occurrences. Such a pre-
incidence of hematomas of wounds,
but, as has already been pointed out, one would not expect such difficulties to be serious.⁴ However, the advisability of the routine use of anticoagulants in

³One of us (R.E.S., Jr.) has subsequently utilized dicumarol with good therapeutic results in a patient before and after aneurysmectomy for an arteriovenous fistula. The distal portion of the artery had undergone thrombosis several days before operation.

the surgery of peripheral aneurysms and fistulas will necessarily depend upon the results obtained after an extensive clinical trial.

With regard to selection of the anticoagulant agent or agents to be used it is apparent that dicumarol has advantages over heparin in cost and in ease of administration in those institutions in which it is economically feasible to provide facilities for accurate daily determinations of blood prothrombin. However if these are not available the drug should never be used for its uncontrolled administration is fraught with great danger. Under such circumstances heparin can be employed more safely. From our clinical experience it would seem preferable to obtain adequate prothrombin levels preoperatively using dicumarol rather than to begin anticoagulant therapy with heparin at the time of the surgical procedure. With this type of program one can avoid the necessity of intravenous administration of heparin during the first few days after operation. It must be pointed out however that our studies throw no conclusive light upon the relative merits of dicumarol and heparin in the prevention of arterial thrombosis. Although we have the impression that anticoagulant therapy played a role in the good results obtained with various methods of arterial repair as we have mentioned previously our cases are not adequately controlled from this viewpoint. Furthermore in all but a few of our patients both heparin and dicumarol were given although heparin therapy was generally of short and dicumarol therapy of long duration. The recent experiments of Kriesewetter and Shumacker¹⁰ demonstrate that thrombosis is apt to occur early after arterial trauma and hence the most critical period is that immediately following operation. It is obvious that the elucidation of the entire problem of the relative worth of dicumarol and heparin in vascular surgery must await further extensive experimental and clinical trial. It is of interest that recent studies in which the two drugs were compared under controlled conditions¹⁰ suggest that heparin is more effective than dicumarol in the prevention of thrombosis after arterial injury and repair. In the light of these experiments and our clinical experience it is suggested that use of both heparin and dicumarol may be the most effective means of carrying out anticoagulant therapy as an adjunct in the surgery of peripheral arteries. It would appear advisable to use heparin at the time of the operation and for the first five or six days thereafter perhaps preferably combined with dicumarol therapy and to continue administration of dicumarol during the following week or two.

CONCLUSIONS

1. Experiences are recorded with the use of anticoagulants and particularly of dicumarol in cases of reparative arterial surgery for aneurysms and arteriovenous fistulas.
2. The methods of administration and of control are discussed as well as the complications which may result from such therapy.
3. The study presented indicates that reparative procedures upon peripheral arteries can be safely undertaken when a full anticoagulant effect has been achieved with heparin, dicumarol or both.

4 Although no proof of the effectiveness of anticoagulants has been furnished, suggestive evidence has been obtained for the belief that such therapy renders less likely thrombosis of the repaired segment of artery

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PULMONARY ARTERIOVENOUS ANEURYSM

A NEW SURGICAL DISEASE

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THE great English anatomist, William Hunter (1718-1783), brother of John Hunter, was first (1761) to describe an arteriovenous aneurysm as 'The simultaneous rupture of an artery and a vein in which the blood flows directly into a neighboring vein (aneurysmal vein), or else is carried into such a vein by a connecting *vie* (varicose aneurysm)'

To date the medical literature contains reports of only ten cases of congenital or nontraumatic pulmonary arteriovenous aneurysm. The lesions have been reported under various titles, such as cavernous hemangioma of lung (seven cases), multiple pulmonary hemangiomas (one case), arteriovenous fistula of lung (two cases). As the gross anatomy in each case is identical and consists of a lobulated, thin walled, branching blood filled pulsating pulmonary sac of varying size made up of both an arterial and a venous component, it seems more accurate and logical to call these lesions pulmonary arteriovenous aneurysms in order to distinguish them from (a) benign hemangioma of the lung, (b) metastatic pulmonary hemangioma of the lung, or (c) hemangioendothelioma of the lung.

Pulmonary arteriovenous aneurysm is truly a rare condition and no account of such a lesion is to be found in the group of world reports of large series of routine autopsies. The first unquestioned case appears to be that reported by Rhodes in June, 1938.¹⁰

As the symptom complex is so definite and typical as to be easily recognized, and cases are being more frequently reported of late it is possible that patients with this disease in the past masqueraded under the erroneous diagnosis of congenital heart disease or polycythemia vera.

A pulmonary arteriovenous aneurysm produces in the lung a shunt whereby a considerable amount of blood passes from the arterial to the venous circulations of the pulmonary circuit without passing through the alveoli of the lung to be oxygenated. The physiologic effect of this is to produce a low oxygen saturation of the arterial blood supply and all the other changes are secondary to this anoxemia.

The extreme rarity of this congenital defect lends zest to a desire for discovering and reporting examples of it. In addition, a patient so afflicted is in constant danger of hemorrhage which sometimes is copious and fatal and cerebral thrombosis with epileptiform seizures due to the slowed circulation and increased red blood cell volume is to be feared. Coronary artery thrombosis also is known to occur. A mild degree of invalidism necessitating curtailment of normal activities is usual, and occasionally venesection and hospitalization are required.

TABLE I ANALYSIS OF TWELVE CASES OF

AUTHOR	SIGNS AND SYMPTOMS											
	AGE (YEARS)	SEX	22 HYPERTENSIVE ATTACKS	PERMANENT CYANOSIS	HEMIPLEGIA	TRAILING	CLUBBING OF FINGERS AND TOES	HEMANGIOMAS ON CHEST	HAEMORRHOIDAL PILES	HEMIPLEGIA	HEMIPLEGIA	HEMIPLEGIA
1. Howes, 1916	2 days	M	0	0	0	+	0	0	+	0	Left	+
2. Poles 1918	25	M	+	+	+	+	0	+	+	0	PML, and LUL	+
3. Smith & Horton, 1939	46	M	+	+	+	0	0	+	0	+	Rt	+
4. Hepburn & Dauphinee 1942	27	F	+	+	+	0	0	+	0	0	Rt	+
5. Gollman 1943	22	M	0	+	+	0	0	+	0	0	Left	+
6. Jones & Thomas 1944	4	F	0	0	+	0	0	+	0	+	RUL	+
7. Jones 1944	20	M	0	0	+	+	0	0	+	+	Both	+
8. Adams & Haines 1944	24	M	0	0	+	Fpx tarsis	0	+	+	0	Left	+
9. Alexander 1945	41	M	+	+	+	0	+	+	+	+	Left & right multiple	+
10. Mahler & Zion 1946	17	M	0	+	+	Fpx tarsis	0	+	0	+	Both	+
11. Watson 1947	27	M	0	0	+	0	0	0	0	0	Rt	+
12. Watson 1947	21	M	+	+	+	+	0	+	+	0	Rt	+

The importance of an early diagnosis becomes obvious when one finds that six patients have been cured by surgical measures. Two of these surgical results form the basis of this report. Surgical measures varying in magnitude from pneumonectomy lobectomy and multiple local excisions to ligation of the offending or 'feeder' artery have been carried out and there have been no postoperative fatalities reported. The patients in each case have returned to their usual occupations. The untreated or medically managed patients have not improved or have died of the complications of their disease.

DIAGNOSIS

If one bears in mind the possibility of pulmonary arteriovenous aneurysm the diagnosis can certainly be established before operation. The reported ages vary from 2 days to 41 years. However, all but three patients were between the ages of 17 and 30 years. The ratio of the sexes is ten males and two females. Persistent cyanosis of the face, hands and feet was noted in ten cases and absent in two. Clubbing of the fingers and toes was noted in nine cases

PULMONARY ARTERIOVENOUS ANEURYSM

TREATMENT													
AGE (IN YEARS)	SEX	HEMATOCRIT (PER CENT)	HEMOGLOBIN	WBC (IN THOUSANDS)	PLATELET COUNT	SPLENECTOMY	PHENYLDIMETHYL- HYDRAZINE	IRRADIATION THERAPY	INFLUOROPAX	T B TREATMENT	ADJUVANT TREATMENT ANY	CLINICAL CASE	RESULT
0	0	0	0	0	0	0	0	0	0	0	+	0	Died
75	0	113%	98	0	0	0	0	0	0	0	+	0	Died of throm- bocytopenic purpura
62	66	23.7 Gm	32	0	Numer- ous	0	+	0	0	0	+	0	Living
96	0	21.9 Gm	0	Normal	0	0	0	0	+	+	0	Pneumo- nectomy	Cured
114	0	137%	41	805 000	0	0	0	0	0	0	+	0	Unimproved
76	0	130%	Normal	Normal	0	0	0	+	+	0	0	Pneumo- nectomy	Cured
0	0	0	114	0	0	0	0	0	0	0	0	Multiple local resections	Improved
80	80	23 Gm	60	0	750 cc preop	+	0	0	0	0	0	Pneumo- nectomy	Cured
82	0	20.4 Gm	76	0	+	+	+	+	0	0	+	0	Died coronary thrombosis
7	55	19.5 Gm	65	1,200 000	0	0	0	0	0	0	+	0	Unchanged
Normal	Normal	Normal	Normal	Normal	0	0	0	0	0	0	0	Ligation on feeder artery	Improved
60	38	17 Gm	60	110 000	Several 1000 cc	0	0	0	0	0	0	Lobectomy	Cured

and absent in three. A high red blood cell count ranging from 6 to 114 million was noted in all but one case (in two cases the red blood cell count is not reported). The hemoglobin varied from 17 to 23.7 Gm and the hematocrit from 55 to 82 per cent. The white blood cell count was normal in each case. The heart was normal in all cases and the electrocardiographic tracings and blood pressure readings when done were not significant. Half the patients reported exertional dyspnea.

Radiographic studies were of great diagnostic value. In each case a branching lobulated mass of uniform density was noted in the lung field and confirmed by tomographic and/or angiocardigraphic studies whenever these were done.

Other diagnostic features were hemorrhage, epileptiform seizures, bruit or heart murmur, a normal platelet count, a normal spleen and normal sternal puncture studies. There was occasionally a history of cough and persistent headaches. In only one case was there a history of trauma (Table I).

TREATMENT

Various medical measures have been employed in the past in the management of pulmonary arteriovenous aneurysm (1) Repeated venesections varying in amount up to 1000 cc brought about temporary symptomatic improvement in four cases (2) Phenylhydrazine was used and afforded two patients temporary relief (3) Artificial pneumothorax was instituted in two cases but the patients were not improved (4) One patient was given a trial of tuberculosis sanatorium regime without success (5) Radiation therapy was of no value in two cases (6) Surgical care was given six patients in three instances pneumonectomy resulted in cure, one patient was apparently cured by lobectomy another by multiple local excisions and in another patient the feeder artery to the arteriovenous aneurysm was isolated and cut between ligatures This patient had no symptoms and returned to his usual occupation but needs observation over a period of years to evaluate the result The procedure in this case was suggested to me by a remark made by Dr I A Bigger in discussing the case of arteriovenous aneurysm reported by Jones and Thompson⁶ He asked the question whether simple ligation of the responsible artery would not be enough to cure the condition This case may give us some clue to the answer

DIFFERENTIAL DIAGNOSIS

Polycythemia vera can be ruled out by the age of the patient, the lack of splenomegaly the normal range of the white blood cell and platelet counts, and the lack of hyperplasia of the white cell progenitors and megakaryocytes in the bone marrow Secondary polycythemia due to high altitude or poisoning by heavy metals or aniline dyes can be ruled out by the history alone and cardiac anomalies with a right to left shunt or chronic pulmonary disease preventing adequate oxygenation may be ruled out by the roentgenographic and electrocardiographic findings

PROGNOSIS

As pointed out by Makler and Zion⁹ the prognosis must be accepted as grave with the danger of massive hemorrhage always present If untreated the secondary polycythemia will lead to serious complications namely exhaustion of the bone marrow with anemia granulocytopenia and thrombocytopenia (Table II)

Thrombosis is a real danger due to the increased viscosity of the blood the increased cell mass the slowing of the circulation and the tendency to clot

TABLE II PROGNOSIS⁹

Theoretically at least, the altered blood factors would tend to place an abnormal burden on the heart.

Duodenal ulcer is found commonly in patients with polycythemia and is said to be due to vascular changes leading to a plugging of small vessels in the intestinal wall.

Half the patients have been treated surgically with excellent immediate results.



Fig. 1.—Case 1 C. E. Chest radiograph showing the lobulated branching density in the right lower lobe.

CASE REPORTS

CASE 1.—C. E., a 2 year old Private First Class, U. S. M. C. R., was due for discharge from the service in September 1915. At that time a routine separation radiograph of the chest revealed a peculiar shadow in the right lower lung field. He had no symptoms and radiographs taken eighteen months previously were said to be negative.

The patient's family history was not remarkable except for the death of his mother at the age of 29 of pulmonary tuberculosis. Past history revealed that he had smoked heavily, taken alcohol in moderation and had suffered two attacks of benign malaria. There was one questionable hemoptysis in 1913.

The patient, a short, heavy, solidly built man weighing 183 pounds appeared normal and healthy. The skin revealed a severe acne vulgaris which was most marked on the back and there was also a diffuse folliculitis of the anterior part of the chest wall. The heart and lung sounds were normal, the pulse rate 78, and the blood pressure 130/85. Laboratory studies were essentially normal, as shown in Table I, Case 11.

Chest radiographs taken Sept. 2, 1945, showed several circular and elliptical densities in the right lower lobe measuring from 2 to $3\frac{1}{2}$ cm in size (Fig. 1). Bronchograms ruled out bronchiectasis and the roentgenologist suggested a diagnosis of lung cyst.

Inspiration fluor and bronchoscopy did not add definite information. The spirogram and vital capacity studies were normal, and the medical evaluation for surgery was reported as good.

Operation was carried out Feb. 28, 1947. The right side of the chest was opened through the bed of the partially resected sixth rib. The right lower lobe was found to be adherent to the chest wall and diaphragm by old fibrous adhesions. In the substance of the right lower lobe, there was a soft lobulated, compressible mass about 4 cm. in diameter which palpated and transmitted a thrill to the fingers (Fig. 2). Entering the posterior costophrenic edge of the lobe, there was an aberrant artery $\frac{1}{2}$ cm. in diameter. When this vessel was compressed the pulsing mass in the lung was no longer palpable. The artery was then followed to its origin from the thoracic aorta doubly ligated and cut across. The lung was then expanded and appeared to be normal. Because the mass could not be palpated and it was believed that the feeder artery had been severed, it was decided that lobectomy was not necessary.

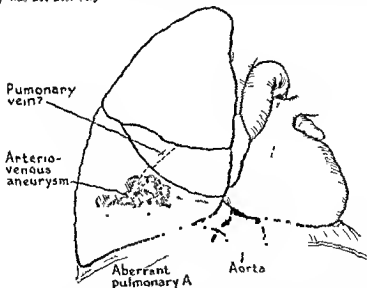


Fig. 2--Case 1. C. Y. Sketch showing the arteriovenous aneurysm. The aberrant artery was doubly ligated and severed near its origin from the aorta.

The postoperative course was complicated by severe diarrhea and persistent abdominal distention. Suppuration occurred in the central portion of the wound probably because of our inability to control preoperatively the severe acne and folliculitis. Culture showed *Staphylococcus aureus* hemolyticus.

The patient was transferred from the Naval Service and at the time of this communication was again without symptoms working at his usual employment. Following operation checkup radiographs revealed the right lower lobe to be unchanged and only on serial films over a long period of time will we be able to learn what has happened to the stagnant blood in the spaces supplied by the ligated aberrant artery.

CASE 2—R. G., a 21 year old Private First Class, USMC, was first admitted to the sick list on August 30, 1945, complaining of dusky color of skin and fingernails of at least one and one half years' duration, shortness of breath on mild exercise for six months, frequent headaches, weight loss of thirty pounds in two years. Bleeding gums and prickly warm feeling over entire body.

The patient's parents, two brothers and one sister were living and well, and there was no familial disease. The father stated that the patient had always had a "dusky" color compared with his other children.

The patient's past history was not remarkable. Specifically he never had scarlet or rheumatic fever, nor other serious illnesses and had never been operated upon. His early life was spent in Denver, Colo., at an altitude of 5000 feet. He had thirty three months' active duty in the Marine Corps with fifteen months overseas. A review of the photofluoroscopic film taken at the time of induction in January, 1943, revealed the pulmonary lesion.



FIG 3—Case 2. R. G. Angiocardiogram showing the vascular anomaly in the right lower lobe.

The patient, a tall, well-built, plethoric man, showed marked cyanosis especially of the lips and face. The retinal vessels were tortuous without evidence of hemorrhage. One small pinhead sized hemangioma was noted in the conjunctiva of the left lower eyelid. Similar hemangiomata were found in the vermilion border of the lower lip, the tip and lateral borders of the tongue, in the bed of one fingernail and in the palms of both hands.

Heart sounds were normal, with a blood pressure of 110/70 and a pulse rate of 72. The lungs seemed clear to percussion and auscultation. The spleen and liver were not palpably enlarged.

Laboratory data revealed red blood cells 6,500,000, white blood cells 6,000 with normal differential, hemoglobin, 17 Gm., sedimentation rate, 2 mm. 1 hr., hematocrit, 58, bleeding

The patient, a short, heavy, solidly built man weighing 165 pounds appeared normal and healthy. The skin revealed a *severe acne vulgaris* which was most marked on the back, and there was also a diffuse folliculitis of the anterior part of the chest wall. The heart and lung sounds were normal, the pulse rate 78, and the blood pressure 120/86. Laboratory studies were essentially normal, as shown in Table I, Case 11.

Chest radiographs taken Sept. 5, 1945, showed several circular and elliptical densities in the right lower lobe measuring from 2 to 3½ cm in size (Fig. 1). Bronchograms ruled out bronchiectasis and the roentgenologist suggested a diagnosis of lung cyst.

Aspiration biopsy and bronchoscopy did not give definite information. The spirogram and vital capacity studies were normal, and the medical evaluation for surgery was reported as good.

Operation was carried out Feb. 29, 1946. The right side of the chest was opened through the bed of the partially resected sixth rib. The right lower lobe was found to be adherent to the chest wall and diaphragm by old fibrous adhesions. In the substance of the right lower lobe, there was a soft lobulated, compressible mass about 4 cm in diameter which pulsed and transmitted a thrill to the fingers (Fig. 2). Entering the posterior costophrenic edge of the lobe, there was an aberrant artery ½ cm. in diameter. When this vessel was compressed the pulsating mass in the lung was no longer palpable. The artery was then followed to its origin from the thoracic aorta, doubly ligated, and cut across. The lung was then expanded and appeared to be normal. Because the mass could not be palpated and it was believed that the feeder artery had been severed, it was decided that lobectomy was not necessary.

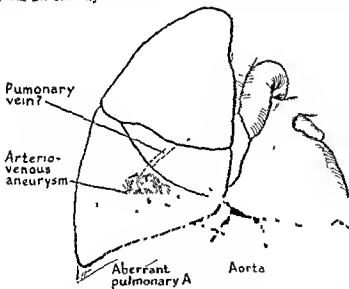


Fig. 2—Case 1. C. L. Sketch showing the arteriovenous aneurysm. The aberrant artery was doubly ligated and severed near its origin from the aorta.

The postoperative course was complicated by severe diarrhea and persistent abdominal distention. Suppuration occurred in the central portion of the wound probably because of our inability to control preoperatively the severe acne and folliculitis. Culture showed *Staphylococcus aureus* hemolyticus.

The patient was recovered from the Naval Service and at the time of this communication was again without symptoms, working at his usual employment. Following operation, checkup radiographs revealed the right lower lobe to be unchanged and only on serial films over a long period of time will we be able to learn what has happened to the stagnant blood in the spaces supplied by the ligated aberrant artery.

and scar. A portion of the parietal pleura had to be excised with the specimen. In the lower anterior portion of the right lower lobe, there was a soft compressible (Fig 4) pulsating mass not well delimited but roughly 5 cm in diameter which transmitted a "thrill" when grasped in the hand. The inferior pulmonary artery was 1 cm in diameter and when ligated and severed the tumor pulsations stopped but the mass remained. A short, wide, 2 by 2 cm, thin walled, pulmonary vein ran transversely from the mass toward the left atrium.

A dissection type of right lower lobectomy was done and the chest wall closed after 100,000 units of penicillin in saline solution were placed in the cavity and the intercostal nerves injected with eucaine. Underwater drainage was used. The patient received 1,800 cc intravenous fluids (1,000 cc whole blood) during the operation.

At the end of the operation the anesthesiologist noted that the patient's cyanosis had disappeared. The postoperative course was fairly smooth complicated only by a thrombophlebitis of the left lower leg vein used for intravenous fluids during operation. He was out of bed on the fifth postoperative day.

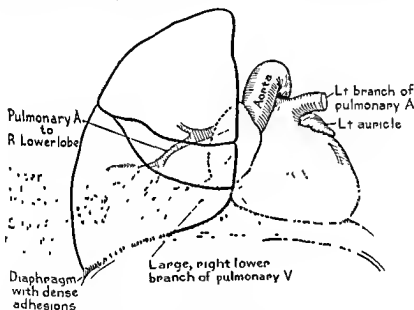


Fig 4—Case 2. R. G. Sketch showing the relationship and relative size and position of the arteriovenous aneurysm.

The specimen was examined and reported as consisting of the lower lobe of the right lung measuring 17 by 11 by 3 cm. Its surface was pinkish gray, mottled with some dark gray areas. The consistency was crepitant throughout. On the lateral surface in the mid portion of the specimen was a suture which when removed showed a venous opening which measured 1 cm in diameter. This was composed of three separate vessels, lined grossly by intima. The lower branch of the right pulmonary artery entered the lung medially. When opened, it was shown to divide into three minor branches, the middle branch of which ran laterally into a multilobulated sinus which measured approximately 3 cm in diameter. The lower right pulmonary vein emerged inferior and slightly posterior to the bronchus. Two branches emerged from the arteriovenous aneurysm which lay for the most part in the lateral portion of the lung. The aneurysm was oval in shape, its long axis being transverse to that of the right lower lobe. Serial section through the remainder of the lung did not reveal any further abnormality. Microscopic findings were reported as consistent with gross findings of arteriovenous aneurysm.

TABLE III LUNG FUNCTION STUDIES SHOWING ARTERIAL OXYGEN CHANGES AFTER LOBECTOMY*

ARTERIAL OXYGEN	REST	AFTER MODERATE EXERCISE
	<i>Before Operation</i>	
Content vol per cent	23.1	21.3
Capacity vol per cent	25.8	26.7
Saturation per cent	90	89
	<i>After Operation</i>	
Content vol per cent	16.8	16.3
Capacity vol per cent	17.5	19.1
Saturation per cent	95.4	91.0

*Case 2 R G—The oxygen saturation has increased to 95.4 per cent.

time 1 min 43 sec clotting time 3 min 15 sec, reticulocytes, 0.6 per cent, platelet count 110,000, icterus index 4 units, CO combining power, 54 per cent, Kahn reaction negative, urinalysis normal, tuberculin test, 1:10,000, negative, sternal puncture studies normal type of bone marrow (2 examinations), electrocardiogram, normal.

The patient was hospitalized and studied for twelve months. Temporary symptomatic relief was obtained several times by phlebotomy of 1000 cc. On Jan 13 1946 he suddenly had a tonic convulsion with transient coma and paralysis of the left arm and leg. Symptomatic treatment was followed by a gradual return of muscular activity and control leaving a residual hypesthesia of the left leg.

Bronchoscopy and bronchography were helpful in eliminating the possibility of a bronchial disorder. Angiography was done on April 12 1946 at Mount Sinai Hospital. After the intravenous injection of 75 per cent diiodrast, roentgenograms were taken and reported as follows: There was a collection of wide vascular channels in the right lower lobe which formed a racemose grouping. The maximum opacity occurred at about four seconds after injection which would suggest that these channels were probably in an anastomotic nature, but there was the possibility of an arteriovenous communication. The main pulmonary artery was normal in size as was the left pulmonary branch. The right pulmonary artery was relatively large. This vascular anomaly was in the right lower lobe (Fig 3).

The lung function unit of the Cleveland Clinic, Columbia University Division of Bellevue Hospital carried out detailed blood volume and oxygen saturation studies prior to and after operation. These findings are summarized in Table III and IV.

Operation was done Aug 8 1946 under intratracheal gas oxygen and ether anesthesia. A right posterolateral incision was made and the chest opened through the bed of the partially resected sixth rib. There was no free pleural space to be found because the parietal and visceral pleuras were sealed to each other by a sheet of old dense adhesions.

TABLE IV LUNG FUNCTION STUDIES SHOWING POSTOPERATIVE IMPROVEMENT IN BLOOD FACTORS*

	BEFORE OPERATION	AFTER OPERATION
Hemoglobin in grams from capacity	19	17
Hematocrit	60	45
Plasma volume (cc per sq m BS)	1,220	1,860
(normal 1,600)		
Total blood volume (cc per sq m BS)	2,400	3,000
(normal 2,800)		
Red blood cell volume (cc per sq m BS)	2,250	1,500
(normal 2,200)		
Vital capacity	52 L	34 L
(normal 150 L plus)		
Maximum breathing capacity	(per minute)	149 L
Circulation time	16 sec	

*Case 2 R G—The hemoglobin, hematocrit and red blood cell volume have returned to normal.

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1st
- 7 Jones R reated
by
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DISCUSSION

Although pulmonary arteriovenous aneurysm is apparently a congenital lesion typical diagnostic symptoms may not appear until the patient reaches the age of 14 years (Makler and Zion),² or 16 years (Hepburn and Dauphinee),³ in one of our patients who had reached the age of 27 years the lesion was causing no symptoms and was discovered only by chance radiography. Alexander's⁴ patient reached the age of 30 before he developed a persistent cough his first symptom.

The diagnosis is suggested by a syndrome characterized by cyanosis, clubbing of the fingers and toes, secondary polycythemia and symptoms of anoxemia usually in a young patient with an obscure lung tumor and a normal heart. A bruit may be heard over the tumor.

It seems certain that trauma does not play an important role in pulmonary arteriovenous aneurysm as a history of injury is reported in only one case in this series. One must assume that a gradual expansive enlargement and thinning out of the walls of the vascular tumor takes place slowly over a period of years and that spontaneous hemorrhage occurs as in Case 2 of this report when some slight overexertion increases the intrapulmonary pressure enough to cause a break. Why this did not result in a massive fatal intrapleural hemorrhage is not clear.

Pulmonary arteriovenous aneurysms are congenital and mechanical defects in the relationship between the pulmonary arteries and veins and as such are not amenable to medical therapy but can be relieved promptly and dramatically by adequate surgical extirpation of the involved portion of lung. There has been no reported operative mortality and the postoperative lung function studies indicate a return to normal factors.

Before operation there is marked hyperventilation at rest during moderate exercise and recovery from exercise. The arterial oxygen unsaturation at rest increases during moderate exercise. After operation the high hematocrit and red blood cell volume decreases to normal and the arterial oxygen saturation improves.

SUMMARY

- 1 The term pulmonary arteriovenous aneurysm is applicable for this group of cases.
- 2 Two cases are reported with preoperative and postoperative data.
- 3 Surgical treatment is urged for every case in which the diagnosis has been established.

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other three were cases of gangrene of the feet, and he felt that in two cases the gangrene spread rapidly as a result of using sodium iodide, necessitating a high amputation in one. Death followed in the other. In 1929, Charbonnel and Masse⁹ favored the use of sodium iodide as a contrast media but mentioned its irritating effects. Edwards¹⁵ felt that there are many disadvantages to sodium iodide.

In 1923 lipiodol was tried by Stead and Forestier¹² in dogs without harm, and in 1927 by Carnett and Greenbaum.⁸ They used 6 cc of iodized oil in the femoral artery of man without harmful effect. They exposed the common femoral artery and passed a tube around it under local anesthesia. They showed excellent arteriograms of the distal vessels, but they were not very



Fig. 1—This arteriogram demonstrates the simplest type of arteriovenous aneurysm with the diodrast going just to the site of the fistula in the superficial femoral artery with no sac. A foreign body is seen at this level. This was confirmed at operation at which time excision of the aneurysm was done.

clear more proximally. It appears to be dangerous since it could cause fat embolism, and visualization of large areas is difficult unless dangerously large amounts are used. In 1930 Saito and associates¹⁷ attempted to remove these disadvantages by emulsifying the lipiodol. They used as high as 20 cc of this emulsion, injecting the carotid, femoral and brachial arteries, and obtained excellent arteriograms.

Roesler¹⁴ stated: A contrast substance injected into the vascular system for the purpose of visualization should fulfill the following requirements. It should contain the greatest possible number of atoms of a heavy element to give sufficient contrast even in dilution. It should be water soluble and have,

PERIPHERAL ARTERIOGRAPHY

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ARTERIOGRAPHY is the roentgenographic visualization of arterial channels by radiopaque media. I have employed this procedure extensively, using 35 per cent diodrast exclusively for peripheral arteriography. This is in contradistinction to visualization of the great vessels such as the aorta and pulmonary arteries, which requires an entirely different technique.^{1, 2, 3} Practically all the arteriograms were done in cases of arteriovenous aneurysms except in certain diagnostic problems. The problems encountered were as follows:

- (1) Determination of arteriovenous communications and the presence of sacs (Figs. 1, 2, 3, 4, 6, 7, and 8)
- (2) Abscess versus aneurysm
- (3) Question of patency of peripheral arteries after injury (Fig. 9)
- (4) Determination of complete thrombosis of aneurysmal sacs
- (5) Determination of the exact communication of vascular masses to the parent artery (Fig. 10)

Historical—Haschek and Landenthal¹ in 1896 reported the roentgenologic visualization of the arteries of an amputated hand and forearm following the intra-arterial injection of a radiopaque substance about eleven weeks after Roentgen discovered the ray. Trendelenburg in 1902 was one of the first to describe an opaque substance within the blood. His patient had been shot in the heart, and on x-ray, the shot could be seen moving to and fro. The first experiments with a liquid medium were done in 1910 by Franck and Alvens² on dogs and rabbits. They used a suspension of lumbric in oil introduced into the heart directly or via the large veins. They then followed the course of these droplets. The earliest good vasograms of the living person were published in 1923 by Berberich and Hirsch.³ They used a 10 to 20 per cent solution of strontium bromide and their pictures were fairly clear. Brooks in 1924 used a solution of 100 Gm. of sodium iodide crystals in 100 cc. of distilled water which had been autoclaved. The solution was injected by direct exposure of the femoral artery at the proximal end of Hunter's canal. Nitrous oxide gas was used during the injection because of severe pain. He reported three cases with arteriograms, and felt that this method was of great value in determining the necessity of amputation in instances of peripheral gangrene, and in determining the site of amputation. He also reported that it could rule out the possibility of arterial obstruction. Singleton⁴ modified Brooks' method by using spinal anesthesia and did not expose the artery. He used the method in six cases. Three were cases of aneurysms and no difficulty was encountered. The

to the use of thorium dioxide sol are observed. It was first reported used as an arteriographic medium in 1932 by Moniz and associates²⁷ who obtained good visualization of the carotid distribution in the head. Dos Santos and co-workers¹² reported on its use in vasography in over forty patients without untoward effect and obtained excellent pictures of the vessels. No one seems to know the ultimate effect of thorotrast. Altogether it is felt that the use of such a drug is undesirable when more suitable and less toxic drugs are available.



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Fig. 1—Th.
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Skiodan was used by Edwards¹, Schuller²⁸, Frey and Zweg¹¹ and Pearse and Warren²⁹. The fact that this drug is used almost exclusively for intravenous urography attests to its safety regarding general toxicity. However it has been my experience that there is considerable pain on the intravascular injection of skiodan. Heathcote and Gardner²⁰ and Pearse and Warren²⁹ have demonstrated experimentally that there is no intimal damage on injection of high concentration (50 per cent) of the drug. Pearse and Warren²⁹ also found this to be true in five of their patients where amputation had previously been decided on and was done. In these the arteries showed no fresh thrombosis or any other evidence of intraarterial damage. Edwards¹² used skiodan preoperatively in varicosities and then examined the tissue removed at operation and found no change.

preferably, a viscosity similar to blood. It should not decompose in the body and should not precipitate with the blood or other constituents of the body. It should not cause local vascular wall damage or spasm or remote, local, general, immediate, or delayed toxic effects. Elimination should be complete and within a relatively short time. It should not be painful when injected and when a paravascular injection occurs, no severe inflammation should result."



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Of all the substances used thorotrast would be ideal but for possible late effects due to radioactivity. It is the molecular weight and not the iodine content of the contrast medium, that influences the degree of radiopacity. Thorotrast is favored by Allen and Camp.¹⁴ It is used in 2.5 per cent aqueous solution of thorium dioxide with the addition of a colloidal solution. Erickson and

"harmful radioactivity
rger amount than that
per extremity. Radt"

introduced thorotrast for the delineation of the liver and spleen in 1930. It can be injected into a vessel without pain or deleterious local effect. He later reported observations on animals and human beings respectively, three and one-half and two years after injection of thorium dioxide solution. Harmful effects were not noted. He expressed the belief that the possibility of harmful effects is largely negligible, providing correct amounts are used and contraindications

Technique of Arteriography—The technique of arteriography involves the transcutaneous injection of a radiopaque media into an artery and making x ray exposures at proper intervals to delineate the desired area. Certain precautions are imperative. This is attested by the results reported by Pendergrass and associates²² which have been mentioned previously. They conducted a survey of deaths following the administration of organic iodine compounds as contrast media in 661 800 examinations, mostly urographic and collected in addition to the eleven previously reported cases, twenty six representing an incidence of 0.0039 per cent. Certain facts are well evident from perusal of the literature and actual experience. It is important to elicit a history of allergy to determine the specific gravity of the urine and to take certain precautions. Diodrast was used exclusively in this series of arteriograms without a serious reaction as well as in a series of phlebograms to which I referred previously.²⁴ A preliminary survey of history of allergy was made and any patient with such a history was carefully observed for sensitivity to diodrast. A high specific gravity of the urine was used as a gross indication of fairly active renal function but if this was low or fixed more careful investigation of renal function was made. A preliminary conjunctival test was employed. This ocular test for sensitivity to diodrast was done as recommended by Harris and Archer⁹ for use prior to intravenous urography. They feel that this is better than the subcutaneous, oral and preliminary small intravenous tests. They used one drop and examined the conjunctiva one and one half to three minutes later. There are three general types of reactions:

- 1 Minimal injection of the conjunctiva—usually the subject will experience a hot flash and some nausea.
- 2 Moderate injection of conjunctiva and scleral vessels—usually the subject will experience nausea, emesis, vasomotor dilatation, occasionally generalized pruritis, urticaria and some slight swelling of the upper respiratory membranes. These are usually temporary reactions and respond readily to the administration of adrenalin.
- 3 Marked injection of sclerae and conjunctiva—this is an absolute contraindication.

If this test was negative 1 cm. of diodrast was injected intra arterially and if there was no reaction within one minute the procedure was completed. One cm. of adrenalin ready in a syringe was always made available before the procedure was started. That this is important is stressed by the report that Pendergrass and associates²² were able to collect in which it was felt that the prompt administration of epinephrine saved the patient's life after a reaction in which the hypersensitivity simulated anaphylactic shock. It is important to palpate the peripheral arteries after arteriography to ascertain any spasm and to treat it immediately.

Upper Extremity Arteriography—A few centimeters of 0.5 per cent procaine hydrochloride are injected over the distal portion of the brachial artery into the skin and subcutaneous tissues. A sphygmomanometer cuff is placed around the arm near the shoulder. The position of the whole upper extremity is abduction and supination. If it is a question of the forearm region alone

Diodrast is one of the newer drugs that has been used extensively for urography and has been given considerable clinical trial in phlebography²⁴ and arteriography. That its use is attended by danger is attested by the report of Pendergrass and associates²⁵ who surveyed the deaths and unfavorable sequelae following the administration of contrast media by sending out questionnaires. They found that twenty six deaths had occurred in addition to those already reported in the literature. The deaths fell into two groups: (1) immediate death due to hypersensitivity or idiosyncrasy to the drug injected or to colloidal shock and (2) delayed death. All of the immediate deaths were due to diodrast but the patients had not received any tests for sensitivity and in



Fig 4.—This demonstrates a huge bilocular aneurysmal sac with an excellently patent artery below the sac only accountable on the basis of an occluded distal venous channel.

only a few had a history of allergy been sought. Nine were done with 35 per cent diodrast for intravenous urography and one (70 per cent diodrast in which two injections of 50 cc each were given) for arterial visualization. Twelve cases were found in the literature and most cases showed immediate cyanosis and cardiovascular collapse with gradually diminishing respirations. Autopsy proved pulmonary edema to be a prominent finding. There were sixteen cases of delayed death presumably due to pre-existing myocardial damage. Leake²⁶ stated: "Diodrast is the sort of compound that may combine with amino acids in the body giving rise to various polyaptics to which sensitivity may arise with resulting allergic symptoms in almost any part of the body. He thought that it should be used with caution where there is any indication of allergic tendency.

arteriography in the presence of arteriovenous aneurysms it is extremely easy to enter the vein rather than the artery because it will be dilated and thickened and will contain bright red blood. This was done in one case (see Fig 5) and merely outlined the femoral vein. Allen and Camp¹ showed in arteriogram of a popliteal aneurysm with sac and an arteriovenous fistula in the region of the middle phalanx of the index finger. Bird reported arteriography in an arteriovenous brachial aneurysm injecting 10 cc of diodrast in the vein in the cubital fossa and compressing the artery proximal to the fistula. He also showed arteriograms before and after eversion of a plantar aneurysm. These were made by injecting 10 cc diodrast directly into the exposed posterior tibial artery.



Fig 5



Fig 6

Fig 5—This demonstrates an easy made error in arteriography of arteriovenous aneurysm. The vein becomes not only dilated but thickened and transmits an active pulsation if a large arteriovenous fistula is near the common femoral vein. In such instances the one may take a false idea that it is the artery. In this case the common femoral

artery is dilated and the aneurysm is a portion of the para-femoral collateral venous channels. The aneurysm proved to be at the site of an aneurysm.

Dos Santos Lamas and Caldas²² listed six items to be determined by the use of arteriography in aneurysm: (1) the variety of aneurysm (2) its relations (3) the permeability of the sac (4) the state of the collateral circulation (5) the exact relation of the arteries and veins in arteriovenous aneurysms and (6) the postoperative result. Horton²³ using 2 cc thorotrast by injecting the femoral artery and compressing the artery proximally, claimed to have been

pronation or a lateral position may be chosen. A posteroanterior projection is used for the visualization of the vessels of the hand. Fifteen cubic centumeters of diodrast are then placed in a syringe and a 19 gauge needle is used to make the arterial puncture. As soon as arterial blood from the brachial artery pulses into the barrel of the syringe the cuff is rapidly inflated above the systolic blood pressure and the radiopaque material is injected. The needle is withdrawn quickly and the first roentgenogram made. The cuff is then deflated quickly to the level of the diastolic blood pressure for a period of several pulse beats to permit the injected material to be carried farther distally. Then the cuff is reinflated quickly to its previous pressure and the second roentgenogram is made. The x ray tube is centered over the expected site of the lesion.

Lower Extremity Arteriography.—It is possible to visualize practically any portion of the arterial system of the lower extremity by injection of contrast media into the common femoral artery and adjusting the x ray tube and Bucky diaphragm to the site to be visualized and delaying the exposure an adequate period. This method is relieved only after a period of trial. It is important to take a preliminary exposure of the area that is to be visualized so that the proper x ray factors will be employed during the injection of the contrast media.

The exposure is best made with the patient in an anteroposterior position. A 14 by 17 film is used. The skin in the femoral region is prepared by shaving and is then sterilized with merthiolate. One half per cent procaine is injected intracutaneously and subcutaneously over the common femoral artery. The artery is palpated and located just distal to the inguinal ligament. Thirty cubic centumeters of 35 per cent diodrast is then put into a syringe and using a 19 gauge needle which is inserted distalward the artery is located. The needle is felt to rest on the artery and can be seen to move with each pulsation. It is then firmly held against the artery and will insert itself into the artery after which bright red blood will spurt into the syringe. The needle is then advanced 1 to 2 cm in the lumen of the artery so that no leakage or disengagement will occur during forceful injection. This injection is done with one hand while the artery is compressed proximally during injection with the other hand. At the end of rapid injection and while still compressing the artery proximally an x ray exposure is made and then another 14 by 17 film inserted after which x ray exposure is repeated following removal of manual compression of the artery. The exposure is delayed according to the distance the dye must travel for proper visualization and by this method the entire major vascular system of the lower extremity including the plantar artery can be visualized. The profunda femoris artery ordinarily will not be visualized unless some obstruction

were done

Arteriography in Aneurysm.—Arteriography was employed extensively to visualize aneurysms and to delineate aneurysmal sacs (see Figs 1 2 3 4 6 7 8 and 10). Technically, it is important to emphasize that in performing

Early Diagnosis of Bone Malignancy—Arteriography is an additional aid in the diagnosis of malignant bone lesions was first presented by dos Santos Lamas and Caldas.¹² Experience has convinced Inclan²³ that arteriography can be of definite assistance in the early diagnosis of malignant lesions of bone provided that the lesion is localized so that the early circulatory changes are evident by x-ray examination. Shulow, Baker and Irv²⁴ felt arteriography to be superior to diagnostic biopsy in the diagnosis of malignant bone lesions since there is danger of spreading a malignant bone tumor by diagnostic biopsy. They agreed with Inclan. Inclan² used thorotrast in doses of 10 to 20 cc. He described the findings in these lesions: (1) filling in of the stroma of the new



Fig 9.—This represents an arteriogram to determine patency of the popliteal artery and core peripheral channels in a case where further operative procedure about the knee was contemplated and it was felt that no procedure was desirable if essential collaterals would be destroyed resulting in loss of limb. A cure was eventually done.

growth by numerous vessels forming a bizarre network and showing extension of the invading tumor (2) the presence of new atypical arterial circulation with pedicles from the main artery and numerous irregular branches entering the bone lesion thus clearly defining the limits of the lesion (3) the premature appearance of a very rich venous circulation with formation of gross venous pedicles arising from the tumor and entering the neighboring vein and (4) an increased arterial circulation appearing distributed perpendicularly to the bone.

Necessity and Level of Amputation—Brooks presented two cases to confirm his impression that arteriography has been of great value in determining

the first to use arteriography to identify an arteriovenous fistula of the femoral artery which was the only accurate means of localizing the fistula except operation. Horton and Ghormley²¹ reported two cases of congenital arteriovenous fistulas visualized by arteriography and felt that these were the first two in the literature. Arteriography overcomes the previous difficulty of locating the abnormal communications. These were in the finger and hand and were treated by surgical means. It is noteworthy that Lewis²² found only thirty cases of congenital arteriovenous fistulas of an extremity recorded in the literature in 1930. In nineteen surgical exploration was attempted in an effort to locate the fistula and this was followed by amputation of the involved extremity in eleven cases.



Fig. 7



Fig. 8

Fig. 7.—This film demonstrates a small arteriovenous aneurysm of the posterior tibial artery. Fig. 8.—This film demonstrates a small arteriovenous aneurysm of the plantar artery and vein. Both films show an arterial aneurysm and emphasize that all such lesions can be analyzed by arteriography.

(58 per cent). Veal and McCard²³ reported the use of arteriography (and the oxygen saturation test) in the diagnosis of congenital abnormal arteriovenous anastomosis of the extremities. They felt that this procedure is of great value. Yater and White²⁴ reported a case of arteriovenous aneurysm with site just below the bifurcation of the brachial artery and showed an arteriogram done with thorotrast. Yater and Otell²⁵ felt that there were few contraindications to the use of thorotrast in quantities used for arteriography. Yater²⁶ reported four cases of aneurysm visualized by thorotrast and felt that this was of great help in acquired arteriovenous fistula.

solved by arteriography, which demonstrated a satisfactory major arterial channel and thus encouraged major surgery in the popliteal space without fear of the loss of the extremity.

Differential Diagnosis—Arteriography has been used to locate the site of embolism²⁸ to detect the presence of arteriosclerosis¹ to determine collateral circulation to detect arterial spasm¹ to detect a torn artery in fracture² and to aid in the diagnosis of thromboangitis obliterans.^{1, 3, 35} I found arteriography of value in one case in which a differential diagnosis between abscess and aneurysm could not be made. Arteriography was done since no murmur could be heard in a swollen leg and aspiration was not conclusive. This demonstrated an aneurysmal sac at the end of a torn posterior tibial artery in a hugely swollen leg. This was removed with a satisfactory result. That an error can be made in diagnosing abscess for aneurysm is demonstrated by reports in the literature.³⁸

Determination of Complete Thrombosis of Aneurysmal Sacs—It is well known that certain aneurysms will obliterate spontaneously. This is determined easily in cases of simple arteriovenous fistulas by clinical means but becomes difficult or impossible in arterial aneurysms. As clotting occurs in a sacular arterial aneurysm it becomes increasingly difficult to determine complete obliteration. This can be easily determined by arteriography and I have used it for this purpose with satisfactory results.

Determination of Exact Communication of Vascular Masses to the Parent Artery—This is well demonstrated by a case of evisoid aneurysm of the medial geniculate vessel secondary to a contusion. Arteriogram (see Fig. 10) accurately outlined the communication and aided in the diagnosis and proper treatment.

Complications—No complications were noted in this series except in one case where the resulting spasm with severe pain required morphine when injecting diodrast in an artery in an individual with arteriosclerosis. This resulted in diminished peripheral arterial pulsation. That this can be a serious complication is noted in a report by Wagner⁴³ in which arteriography in the upper extremity in a child aged 14 months resulted in marked ulceration following persistent absence of the radial pulse which must have resulted from thrombosis.

Complications following arteriography are most prone to occur at the two extremes of life because in infancy and childhood the vessels are particularly susceptible to spasm those of the upper extremity more so than the lower and because in old age the incidence of arteriosclerotic occlusion is increased and the collateral circulation becomes progressively worse. Trauma to the artery is a result of puncture by the needle and the force of injection by arterial distention may in themselves provoke reflex vasoconstriction. The reactions may be local or systemic. The local reactions consist of hematomas extravasations and thrombosis. The more remote effects are severe vasospastic reactions hemateme- sis anemia flushing of skin erythematous eruptions nausea vomiting cyanosis respiratory distress and fall in blood pressure death from allergy and hypersensitivity.

A hematoma may occur at the site of arterial puncture but this is usually easily prevented by aspiration on withdrawal of the needle and then firm digital

the necessity of amputation in instances of peripheral gangrene and, in those instances in which amputation was indicated, in determining the site at which amputation should be done. Peirce and Warren²⁵ reported two cases in which amputation was not done because the arteriogram showed patent vessels. Schuller²⁶ reported a case in which arteriography was very helpful in deciding the site of amputation in a case of arteriosclerotic gangrene, where clinical tests showed vascular insufficiency up to the knee and no peripheral pulses could be felt, yet the arteriogram showed a patent peroneal artery.



Fig. 10.—This arteriogram visualizes a circumscribed aneurysm of the superior medial genicular artery and on the original film demonstrated the communication with the parent superficial femoral artery.

Question of Patency of Peripheral Arteries After Injury—Not infrequently the question arises as to the necessity of determining the patency of a peripheral artery following injury. It is desirable to determine this where so-called 'critical arteries' are involved. In the extremities one of major considerations is the popliteal artery. In one such instance (see Fig. 9) there had been marked damage to the structures in the popliteal region from previous fracture. Further major operative procedure was contemplated regarding neurovascular repair and it was clinically impossible to determine popliteal arterial patency. This was

- (3) Location of the site of an arterial embolus
- (4) Determination of collateral circulation
- (5) Outlining of arterial injuries and determination of patency following injury
- (6) Differential diagnosis of abscess and aneurysm
- (7) Determination of thrombosis of saccular arterial aneurysms
- (8) Determination of communications to vascular masses of the parent vessel

It is recognized that there are certain dangers to arteriography, but careful adherence to detail will avoid complication. It is felt that the procedure is a valuable one and deserves much consideration. Despite often repeated statements that such a procedure is unnecessary because clinical diagnostic methods are adequate, it is felt that such individuals are overlooking an easily performed and valuable adjunct to diagnosis and treatment.

Acknowledgment—The patient reported in Fig 10 was operated upon by Dr W E Rector and the author wishes to acknowledge his help in securing several of the arteriograms reported.

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pressure for one minute. It usually absorbs spontaneously. No such incident occurred in this series. Demel¹⁰ stated that in arteriosclerosis in one out of 300 cases there may be bleeding from the artery, readily controlled by a suture through the adventitia. Dos Santos and associates¹¹ among 1500 arterial punctures had only one case of persistent bleeding necessitating ligation of an atheromatous femoral artery, and the patient recovered without gangrene of the extremity. Extravasation of the contrast media should rarely occur. Displacement of the needle can occur, however and in 411 arteriographies with the use of thorotrast Dos Santos¹² had only eight extravasations. Dimitza and Jaeger¹³ among seventy transcutaneous arterial injections had six extravasations but they were not followed by serious consequences except nausea and fever. Absorption and resolution of the resultant inflammatory process is slow. Diodrast will usually absorb but thorotrast may diffuse by way of the lymphatics and slowly form a mass some distance from the original site of injection. Dos Santos¹⁴ reported the development of suppurative mass in the iliac fossa two years after femoral arteriography with thorotrast complicated by extravasation of the contrast media.

Among the serious complications are severe immediate vasospastic reactions in the injected limb. In almost all instances these have followed the use of organic iodine compounds rather than thorotrast. Dos Santos¹⁵ in 129 arteriographies with organic iodine compounds had six cases in which gangrene was aggravated in contrast to no vasomotor reaction in more than 300 with thorotrast. The vasomotor reaction is manifested first by severe pain in the limb and blanching followed by venous stasis. Later scattered violet plaques may occur. Motor paralysis may occur skin and tendon reflexes may be abolished and anesthesia may be present distal to the zone of injection. The pain usually subsides in two or three days. The evanescent plaques slowly resorb passing through the colors of a hematoma and blisters may occur. Movement and sensitivity gradually return and in a week to ten days the limb may become normal. In other cases a pre-existing gangrene may be aggravated.

In a few instances the puncture site has been surgically explored. The muscles are engorged with dark blood which flows readily from the veins but does not spurt from — there

is no hematoma.

Laveuf¹⁶ the artery

blood. On opening the artery a soft clot is formed which does not prevent passage of the needle into the lumen of the vessel. The arterial lumen often contains a recent thrombus undergoing organization.¹⁷

CONCLUSIONS

Peripheral arteriography is a valuable adjunct to the diagnosis and treatment of arterial lesions. The following indications are recognized by the author:

- (1) Visualization of aneurysms and fistulas and delineation of aneurysmal sacs
- (2) Early diagnosis of bone malignancy

CHRONIC EVENTRATIONS AND LARGE HERNIAS

PREOPERATIVE TREATMENT BY PROGRESSIVE PNEUMOPERITONEUM— ORIGINAL PROCEDURE

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DURING May 1940 an obese woman aged 65 years suffering from heart disease was admitted as an emergency case because of large incarcerated supraumbilical eventration without obstruction. The patient was in poor general health. Under careful observation she was given two small intraperitoneal injections of oxygen and after one week the incarceration disappeared. A fortnight later following repeated insufflations of oxygen she was operated upon under local anesthesia and both the operation and the imbricated iponeurotic closure were performed without difficulty. The postoperative course was uneventful.

At the Twelfth Argentine Surgical Congress (October 1940) in a paper on Postoperative Eventration presented by Professor J. M. Jorge and me the following statement occurred:

Although our present experience only allows us to bring a preliminary report to this Congress one of us (Gomi Moreno) has attempted the preoperative preparation of cases with chronic postoperative eventration or gigantic hernias with a method which we have not found previously recorded. It consists of a *progressive pneumoperitoneum* with injections of oxygen.

This was apparently the first time that a pneumoperitoneum had been used for therapeutic purposes in eventrations and hernias. It had been used previously only in the treatment of certain forms of bowel and peritoneal tuberculosis and both in radiographic and laproscopic diagnosis.

Since 1940 my assistants and I or other Argentine and South American surgeons have operated upon approximately fifty patients of both sexes with large neutral hernias usually uncomplicated who had been prepared by this procedure. No accidents occurred and the procedure has the advantage of being simple and efficient.

Professor Manuel Riveros of Paraguay has informed me that he already has five successful cases to his credit and is very enthusiastic about this method.

I understand that it is being used satisfactorily in various surgical departments in Argentina, Uruguay and Chile.

Few publications have dealt with the method. In 1944 two senior physicians in my department brought this subject up to date in a communication read at a meeting of the Argentine Society of Surgeons†. The same year

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respiration disorders, and the lack of sufficient thoracic respiration produces a poor postoperative risk

By preoperative intraperitoneal air insufflation the postoperative changes that is increased intra abdominal tension diaphragmatic elevation and respiratory difficulty, are produced but to a minor degree. For this reason the first injection should be done cautiously although the disturbances it produces usually disappear rapidly. The second and third injections are generally well tolerated and the amount of air and pressure may be increased considerably. A remarkable feature of pneumoperitoneum is that in spite of the greatly increased intra abdominal pressure there is no reduction in the patient's vital capacity as determined by spirometry.

The patient can be given four to five sessions of *progressive pneumoperitoneum* over a period of three to four weeks and in quantities that in the last session may reach the extraordinary amounts as much as 6 to 8 L and pressures of 30 to 40 mm on Claude's scale whereas in the same patient 500 to 1000 cc as initial dose would have produced marked symptoms due to abdominal hypertension such as dyspnea and pain in the left shoulder even though the intraperitoneal pressure did not rise above 10 mm. The patient's vital capacity which before treatment may be 1500 cc is likely after the first injection to decrease to 1000 cc but later will rise and become stabilized between 1500 and 2000 cc by the end of the treatment.

When the abdomen is opened and all the air expelled the patient has a feeling of relief the abdominal walls become flaccid and the viscera show no tendency to protrude. The operative closure is much easier than when deep anesthesia is used. Moreover aponeurotic imbrication is easy and the sutures are not subjected to tension.

I have operated upon some patients under local analgesia just to prove that this is possible. In a large eventration in an obese woman I have used 600 cc of a 1 per cent solution of percaine. Spinal or general anesthesia are preferable however.

The dissection of the sac and liberation of adhesions becomes easy because of the stretching produced by the preoperative air pressure.

Vital capacity improves with the release of the air and breathing becomes freer the postoperative course is uneventful.

Neither I nor other surgeons who have followed this technique have seen a single pulmonary or venous complication in the large number of large eventrations treated. I have had no complication resulting from insufflation of the peritoneum. The method is harmless and has many advantages and I would even go as far as to say that it solves all technical and postoperative difficulties.

It is however contraindicated (a) in aged patients in poor health with diabetes and uremia etc unless they are emergency cases in which all other forms of treatment have failed in relieving a strangulation and even this may fail (b) in decompensated heart cases (c) in blocked or strangulated hernias or eventrations which have existed for several hours.

report was made* on the successful use of the method in the case of an elderly woman who was admitted in severe shock and suffering from a strangulated postoperative hernia

Progressive pneumoperitoneum has occasionally been used in chronic complicated eventrations and in those cases only to obviate an emergency but its real indication is in uncomplicated cases as a means of preoperative preparation

Rationale of the Procedure—Two questions arise concerning the mechanism by which repeated pneumoperitonea are efficacious in large neutral hernias. Is it a substitute for the weight reduction therapy or does it permit an adjustment of respiratory balance?



Fig 1—Pathologic state in a chronic eventration

In the first place it acts upon the disproportion between the abdominal container and its contents most of which are lodged in the large sac originally described as 'the second abdomen'. Were the distended viscera, omenta, fatty and edematous mesentery—all of which have lost their 'rights of domicile'—suddenly returned to the abdominal cavity, not only would this produce embarrassment by increasing the abdominal contents but also the closure of the peritoneum and other parietal layers would be difficult and the sutures would be subjected to excessive tension, hence the fear of recurrences.

Second, the postoperative condition of the patient would be hindered by the effects of the sudden increase in abdominal tension in a patient whose breathing is already deficient. Obesity with its tendency to pulmonary complications and phlebothrombosis resulting from chronic venous stasis increase

*Ottolenghi, E. L. El neumoperitoneo en la reducción de la eventración post-operaria estrangulada (comunicación previa). *Diagn. y Trat.* 16: 1149-1150, 1944.

Some will suggest that an intensive reduction in weight and well controlled breathing exercises will prepare the patient satisfactorily for operation

Even when this is done it must be recalled that at times it is necessary to crush the phrenic nerve in order to increase the abdominal capacity

It has not been an easy matter to solve the problem. My own earlier experience (prior to using pneumoperitoneum) had convinced me that the treatment based on weight reduction was insufficient. It will reduce the weight of an obese person weighing 270 pounds by some fifty pounds which will make little difference in the local conditions besides it is a very protracted treatment that is seldom tolerated by the patient because of various reasons the financial one being one of them

The treatment I suggest lasts at most from two to three weeks. Although I have always kept the patients in bed I believe it could be carried out as an ambulatory procedure

Preparation of the Patient—The patient should not take any food during several hours prior to the treatment. Although it is not necessary to be too severe in this respect it is important to perform the pneumoperitoneum some time after food ingestion because of the digestive disorders that can appear. Once admitted to the ward the patient should be placed in the Trendelenburg position. Well controlled breathing exercises should be carried out duly by means of a spirometer and the various readings must be recorded on a chart for future reference

A careful observation of patients treated by pneumo injections enabled us to establish that a large proportion of the gas entered the second abdomen formed by the eventration through the defect in the aponeurosis of the abdominal wall. This escape of the gas into the hernia nullifies the purpose of the pneumoperitoneum (a uniform abdominal pressure) since the tension becomes much higher in this region than in the rest of the abdomen. This difficulty can be solved before beginning the treatment by using a procedure very similar to that applied by pediatricians in the treatment of umbilical hernias in babies. After applying benzoin tincture to protect the skin of the abdomen the hernia is reduced by invaginating the sac along with a fold of skin and bringing the sides of the opening as near together as possible. While they are held in this position an assistant applies several strips of wide adhesive tape across the abdomen the width and position of which bear a direct relation with each individual case and the surgeon's dexterity. The important feature is that they should produce as near as possible the ideal objective—the closure of the hernial sac. In the patients who are not confined to bed the upper edge of the horizontal strips of adhesive tape may produce ulceration of the skin which can be prevented by not allowing the patient out of bed even for a short time, without wearing a tight body bandage.

With this simple procedure we have had no mishaps in over 300 pneumoperitoneum injections in eventrations of all sizes and of the most capricious shapes and which have been injected with as much as 8 L. of air in one

As a *relative* contraindication—which means that one must act *cautiously*—we must consider the chronic eventrations with a narrow ring that have undergone repeated incarceration and strangulations. Even in such cases the pleating of the sac by means of adhesive tape and bandaging will allay any acute hazard. I draw attention to this contingency because of an experience with one such case.

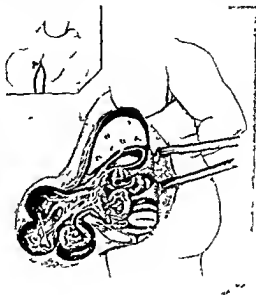


Fig. 2—During the treatment

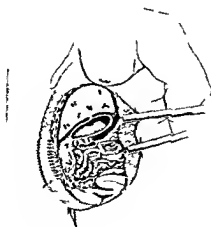


Fig. 3—After operation no suture tension can be observed

in the neighborhood of that of the previous injection (in the event of it being the first injection, it is the highest amount of air tolerated by the patient without discomfort) The ideal is to be able to inject more but this is not always possible, *one must not insist in doing so* but must consider the patient's tolerance

On some occasions during the first or successive injections a few difficulties may arise such as acute pain like a stab near the puncture zone which may radiate toward the corresponding hemidiaphragm This contingency appears suddenly and disappears in the same way if the injection is stopped for a few minutes after which it may then be resumed successfully

THE INJECTION OF AIR

So long as their mechanism of production is understood this dual feature of both sudden onset and disappearance of pain and its short duration is the best sign for differentiating the slight and passing handicaps from those that indicate that the patient's tolerance peak has been reached

When the aforementioned contingency appears after a brief pause the air injection should be continued as slowly as possible controlling the rate of air passage by means of a Richardson's insufflator

If on resuming the injection after the pause the pain reappears with identical characteristics a further pause may be tried however should the disturbances continue the session must be postponed until another day

Should everything go well the air can be injected at a rate of 1 L. (10 $\frac{1}{2}$ pints) per 1 $\frac{1}{2}$ minutes and continued until the patient begins to complain of the following disorder: (a) uncomfortable distention and (b) diffuse pain that begins at the site of puncture and then affects the whole of the abdomen in a more or less capricious way It is usually more marked in the right flank over the pubis and the left hemidiaphragm occasionally the pain extends to the left shoulder

These are the signs that should be recognized and given due consideration by anyone who attempts a pneumoperitoneum and wishes to obtain its full benefits

In order to decide when a session should end one of two methods may be followed either the injection of air must be continued until the aforementioned disorders appear or the useful pressure is determined beforehand according to the results of earlier injections namely an equivalent or slightly larger dose

After registering the pressure the needle is withdrawn, the puncture covered with cotton wool dipped in collodion or alcohol and a body bandage is applied

After a five minute pause to allow the patient time to quiet down the breathing is controlled by spirometry and the session is over

After the administration of a pneumoperitoneum patients are given very little food (the appetite is generally low) and on no account are they allowed to get up until the next day

single session (Case 39624) attaining an intra abdominal pressure of 32 cm on the Claude manometer

Before starting the administration of the pneumoperitoneum, we carry out a careful examination to estimate the patient's general state of health, to establish the operative chances, and to determine whether the pneumoperitoneum may be undertaken without any risks. Also prior to the injection, obese patients should be kept in bed for three or four days in a moderate Trendelenburg position, breathing, lower limb exercises, and massage must be carried out twice daily and a convenient calorogenic diet prescribed.

Moreover, during the three or four days that precede the first session of pneumoperitoneum, the bowels should be emptied by daily enemas.

Technique of Air Injection—The patient lies on the back, in a moderate Trendelenburg inclination. The strips of adhesive tape are applied or renewed, as the case may be. Spirometry is then determined.

The surgeon, wearing sterilized gloves, applies the antiseptic solution to the skin of the left iliac region of the abdomen. Under procaine anesthesia a wheal is raised in the middle of a line joining the anterior superior spine with the umbilicus. A spinal puncture needle is introduced into the abdominal wall until it reaches the peritoneal cavity, that this has taken place is confirmed by a special sensation of going through a resistance which has opposed its progression. In the case of a first puncture, or when it is thought that owing to the long time lapsed since the last one there is no remaining gas, a small amount of air should be injected by means of a syringe. If this is done easily it is almost certain that the point of the needle is within the cavity. Provided it is not the first injection, we systematically connect the needle to the apparatus used to supply the air, the manometer will register the pressure of whatever residual air there is in the abdominal cavity.

Once it is certain that the needle is in the right place and the pressure has been noted, air is slowly injected its pressure and rate being regulated by means of Richardson's insufflator.

When it is desired to know the amount of air that has been injected (a purely documentary interest, because what is important is the intra abdominal air pressure and not the number of liters) we use two saline solution bottles, one full of water and the other empty. The air injected by a Richardson's insufflator will alternatively force the water from its container into the other bottle and thus inject an equivalent amount of air into the abdomen. The size of the bottle (500 cc in our department) multiplied by the number of times this amount has been injected will give an idea of the size of the injection. If we also wish to know the pressure, the abdominal cavity can be connected with a manometer by means of a two way key.

The elimination on one of the bottles saves time as it avoids both changing the tubes backward and forward from one bottle to the other and the need of an assistant.

From time to time the manometer is connected so as to control the pressure reached and thus estimate when the useful one is obtained—somewhere

namely, the time when he considers that from the abdominal and respiratory point of view, the patient is most fit to undergo the operation

After one has acquired a certain experience in pneumoperitoneum technique, both a comparison between the abdominal distention when pressure reaches its peak, as compared with that before injection and the flaccidity of the abdominal walls in this condition, if correctly interpreted, will provide very important data for making this decision

The moment vital capacity becomes stabilized or rises slightly after four or five sessions and the patient realizes that he breathes more freely, it can be considered that the preparatory period is about finished

Earlier in our experience, occasionally patients complained of pain during the air insufflation which was due to the gas being injected at excessive pressure and rate producing a "surprise reflex" much stronger than normal, and giving rise to a painful contraction making it impossible to continue with the injection. As we now inject the air very slowly (1 L. per $1\frac{1}{2}$ minutes), we have never had to suspend the treatment

The treatment usually lasts two to three weeks, in which the patient receives five to six injections (one every five days). Besides using pressure control and the number of liters injected as a physical index we take progressive spirometry as a physiologic index of vital capacity. Although this last index does not always follow a parallel course to the progress of treatment it must be admitted that owing to a purely mechanical factor there is a drop in the vital capacity of a patient subjected to a high intra abdominal tension. However, if daily spirometric readings taken during the breathing exercises do not show a reduction it is because the treatment is following a very good course. This index will be all the more valuable for establishing an improvement in pulmonary ventilation, when vital capacity increases by 500 to 1000 cc before removing the intraperitoneal air because it would mean that once the obstacle to free diaphragmatic excursion has been removed spirometry will register a marked increase in vital capacity.

Later on (between twelve to twenty four hours) patients may present certain disorders, such as dyspnea, palpitations, headaches, and back pains all of which will disappear rapidly by returning the bed to horizontal position and by the administration of $\frac{3}{4}$ to $1\frac{1}{2}$ gr of phenobarbital

The technique just described makes it evident that the real guide to the course of this treatment lies in the figures resulting from research done on intra peritoneal pressure

However, we have not yet been able to apply this criterion as a matter of routine because of the difficulty in obtaining good tensiometers of late. Notwithstanding, we have decided to follow the criterion based on the pressure record and not on the amount of gas injected for the following reasons

1 Because the useful effect is not determined by the number of liters injected but by the pressure which the gas exerts on the abdominal wall

2 Because there is no direct relation between the number of liters injected and the intraperitoneal pressure. This assertion is further supported by the fact that it is influenced by many other causes such as size elasticity and tone of the abdomen and its walls. It must also be remembered that the injection of 2 L. of air will not have the same effect in the first session as in the fourth or fifth because in the latter the abdominal walls have already attained a certain degree of relaxation and their tolerance has increased

3 Tensiometry also enables us to determine the presence and amounts of residual air while if the number of liters injected in the previous session were the only source of estimation it would never be possible to ascertain the new amounts to inject

Besides being the only useful figure pressure readings may be obtained with accuracy at any moment and will thus allow comparative determinations *

4 Time that should elapse between successive sessions. No figures can be given as a fast rule as the intervals depend on certain individual factors on the part of the patient such as tolerance rate of absorption etc moreover there is also the surgeon's criterion to be considered

If the useful pressure lies in the neighborhood of that reached in the previous session but it is found that there is a steady decrease through absorption the only way in which it can be maintained more or less stable is by more frequent injections. This would be the ideal preoperative technique but in practice there are numerous difficulties and our own experience tells us that the best results are attained with an interval of roughly five days between injections. Although we do not claim to make a fast rule of this five day lapse, both periodical abdominal palpations revealing a certain relaxation, and the control of pressures have led us to consider it the most appropriate one

5 Operative opportunity is an interesting point as two sets of factors must be taken into account the individual patient and the surgeon's criterion

*These results estimated by the pressure readings are the fruit of a careful study carried out by one of my assistants Dr Juan C Aguilar



Fig. 1—Facies of Cushing's syndrome

CUSHING'S SYNDROME ASSOCIATED WITH FUCHSINOPHILIC STAINING REACTION IN THE ADRENAL

ARTHUR H. PEDERSEN, M.D., and THOMAS J. KENNEDY, M.D.
ST. PAUL, MINN.

MOST of the standard textbooks of medicine and pathology describe Cushing's syndrome as one in which there is the painful obesity of the face, neck and trunk, early amenorrhea in females and ultimate sexual impotence in males, hypertrichosis of the face and trunk in females and preadolescent males, loss of hair of the scalp, dark red striae of the skin especially on the abdomen, hypertension, diminished sugar tolerance often with hyperglycemia and glycosuria, osteoporosis with pain in the bones and general bodily weakness.

Some of the pathologic findings associated with Cushing's syndrome or the adrenogenital syndrome reported are: adenomas and carcinomas of the adrenal cortex, hyperplasia of the adrenal cortex, fuchsinophilic granules of the cells of the adrenal cortex, basophilic adenoma of the anterior lobe of the pituitary, arrhenblastoma of the ovaries, granulosa cell tumors of the ovary, tumors of the pineal body, and tumors of the thymus.

The case is presented because of its surgical interest and the hyperplasia of the androgenic zone noted in the adrenal made manifest by the fuchsinophilic staining reaction. No other pathology could be demonstrated by crural or exploratory laparotomy to account for the Cushing's syndrome. Oppenheimer and Silver reported the finding of these fuchsinophilic granules in virilism but also in adenomas of the adrenals found incidentally at post mortem. Cahill and his co-workers reported finding these granules in the adrenals of dogs and in human beings without virilism; however, the granules were more marked in adrenal cortical tumors with virilism. Sudds has demonstrated these granules in 24 per cent of adult males and in 28 per cent of adult females. Several controls were examined in this case—ranging from the newborn infants dying of atelectasis of the lungs to patients in the older age groups dying of coronary thrombosis and in no instance did the fuchsinophilic staining reaction approach that of the adrenal in Cushing's syndrome. In the newborn infant the fuchsinophilic granules were almost completely absent; in the older age groups they were of a spotty type. Vines, by examining some sixty fetuses, dem-

female—the reaction was less marked in the female.

At the end of twenty weeks this disappeared. In addition Vines found of the pituitary, the interstitial cells of the testis and the cells of the young corpus luteum. In 1934 Broster reported a series of fifteen cases of the adrenogenital syndrome in which he described the fuchsinophilic reaction in nine of them as strong in three of them.

as moderate, and in the remaining as fairly marked. He divided the cases of adrenogenital syndrome into three types. In Group I were included the cases of adrenopseudohermaphroditism; in Group II were included the cases of adrenal virilism—changes were noted after puberty; in Group III were included the cases of mild virilism. Of Broster's fifteen cases, eleven belonged to Group II. Following a unilateral adrenalectomy, there was a moderate improvement in most of these patients. The male characteristics disappeared, the menses became regular, and there was a disappearance of the hirsutism. As the result of the work of Broster and Vines it was felt that a special staining reaction associated with clinical masculinization of the female had been discovered, and the staining reaction was present temporarily in the cells of the adrenal cortex of both sexes in the early stages of fetal life. The case presented here corroborates the work of Broster, Vines and other investigators, in that a rather marked fuchsinophilic staining reaction was noted in the adrenal resected.

CASE REPORT

Mrs. G. M. was admitted to St. Joseph's Hospital Sept. 16, 1946, and discharged Oct. 25, 1946. On admission the patient was complaining of dryness of the skin, increase of hair on the body, and insomnia. She stated that in March 1945 she had noticed the first "symptom" which she described as a bloating of the stomach and insomnia, increasing in severity as time went on. In July 1945, she was told by her mother that she was gaining in weight, and that it was particularly pronounced in the face, neck and shoulders. She also noticed at this time that the lips and legs were swelling. In January 1946, the obesity of the face, neck and shoulders became conspicuous, and in addition, her hair began to thin out and became very dry. However, at this time she noticed hair appearing on the face, arms, legs, back and buttocks. It was at this time that the menses which had previously been scanty and irregular ceased entirely. In January 1946 the skin gradually became coarse and scaly, and she also noted a marked diminution of libido while the breasts were becoming atrophic. Three months prior to hospital admission she developed a marked back pain which persisted up to the time of admission. Her father and mother were living and well as were three sisters and one brother. The patient had a tonsillectomy at the age of 14 years. There were no other serious injuries or diseases. Past history revealed she had had a normal pregnancy in 1941 with the delivery of a normal female child.

Physical Examination.—The general appearance revealed a well developed, well nourished white woman. The skin of the entire body appeared scaly and rough. There was a male distribution of hair except on the chest. Examination of the pupils revealed reaction to light and accommodation. The ears, nose and throat appeared normal. The hair of the scalp appeared to be thin and the scalp scaly. Examination of the chest showed the lungs clear to auscultation and percussion. The neck and shoulders appeared to have much fat. A lump was noted between the scapulae. The breasts appeared atrophic. Examination of the heart revealed the tones to be clear in rate and rhythm regular. No murmurs were heard. The blood pressure was 180/110. Examination of the abdomen did not reveal any palpable masses. Examination of the extremities revealed an unusual amount of hair on both arms and legs. The reflexes appeared normal.

Laboratory Findings.—On admission to the hospital, a urinalysis showed the specific gravity to be 1.009. The remainder of the examination was negative. On September 26, the blood calcium was 8.7 mg. per 100 cc. The blood serum potassium was 45.4 mg., the acid phosphatase 1.83 units, the alkaline phosphatase 20.85 units (King-Armstrong units). On October 18, the blood serum potassium was 39.7, the acid phosphatase 1.5 units, the alkaline phosphatase 13 units (King-Armstrong units).

In March 1946 the patient was registered in Ancker Hospital, St. Paul, at which time further laboratory work was done. A glucose tolerance test, at this time, revealed a fast

Fig. 4



Fig. 4—Nuclei of cells stained with Eosin
Fig. 5—Stained cells stained with Eosin

of blood sugar to be 170 mg per cent. The first hour was 230, the second hour 304, the third hour 311, the fourth hour 240 mg per cent. On another occasion the fasting blood sugar was reported as 178 mg per cent. A spinal fluid examination revealed the pressure to be 160 mm water. The total protein was 72.2 mg per 100 cc and the Wassermann and the colloidal gold were negative. The hemoglobin was 13.6 Gm per 100 cc, the leucocyte count 11,300 with 1 lymphomonuclears 8 per cent, lymphocytes 11 per cent and monocytes 2 per cent. A blood cholesterol was 269 mg per cent. The blood chlorides were 670 mg per cent. On April 19, 1946, a 17 ketosteroid determination on a twenty-four hour urine was reported as 11 mg. The basal metabolic rate was minus 7.3 per cent and the Van Slyke 67 volumes per cent.



Fig 2

Fig 2—Air injected right renal area
Fig 3—Air injected left renal area



Fig 3

X-Ray Findings—In March, 1946, when the patient was at Ancker Hospital, roentgenograms of the chest and skull were reported as negative. On admission to St. Joseph's Hospital, air was injected into the left perirenal space and no evidence of tumor could be noted. A few days later the right perirenal area was examined by the injection of air and reported as negative to tumor. At this time, fractures of the right ninth rib and the left eighth and ninth ribs anteriorly were noted. There were swelling and a bony callus was present. Compression fractures of the bodies of the eighth and ninth thoracic and first lumbar vertebrae were also noted and all the bones showed marked decalcification.

Operation—On Oct. 5, 1946, an exploratory laparotomy was performed. The ovaries were noted to be somewhat atrophic but the uterus appeared normal. Careful palpation in the pelvis and along the vertebral column and ureters on either side revealed no evidence of tumor. Both adrenals were palpated and because the right adrenal felt larger than the left and small nodules could be felt on it, one-half of it was resected.

Fig. 1



Fig. 2

Fig. 1—Section of adrenal gland stained with iron-haematoxylin.
Fig. 2—Section of adrenal gland stained with iron-haematoxylin.

Pathologic Findings—The adrenal presented no unusual gross abnormalities. Sections were made and stained with the Ponceau fuchsin stain. The technique of the Ponceau fuchsin stain consists in fixation of the tissue in a 25 per cent solution of potassium bichromate and a 1 per cent sodium sulfate. The tissue is embedded in paraffin following which it is stained for five minutes in a solution of 1 part of a 1 per cent acid fuchsin and 2 parts of a 1 per cent Ponceau DeXylidme. It is then washed in distilled water and differentiated for five minutes in a 1 per cent solution of phosphomolybdic acid. The tissue is then placed in a 25 per cent solution of aniline blue after which it is washed in distilled water and then differentiated in 1 per cent acetic acid. The tissue is then mounted in balsam. Normal adrenal cells for the most part absorb the aniline blue stain. The androgenic cells take up the red acid fuchsin stain. The adrenal in this case presented a rather marked fuchsinophilic staining reaction which was most pronounced in that part of the cortex adjacent to the medulla. In some areas the fuchsinophilic cells were noted extending from the juxta medullary zone to the zona glomerulosa such a zone is shown in the photomicrograph (Fig 5).

Progress in Hospital—Prior to surgery the patient appeared emotionally upset and depressed at times. In conversation her remarks were occasionally incoherent. Following surgery the patient made an uneventful recovery. She was given deep x ray therapy to the pituitary and on Oct 29 1946 was sent home. About four weeks after leaving the hospital she had a small amount of vaginal bleeding and eight weeks after hospital discharge she had a normal menstrual period—the first in almost two years. At the time of this communication there had been a moderate improvement in mental condition.

SUMMARY

A case of Cushing's syndrome is reported in which the only significant pathologic finding is a rather marked fuchsinophilic staining reaction in the adrenal. The same stain applied to the controls did not reveal this degree of fuchsinophilic staining reaction.

Following surgery which must of necessity have destroyed a greater portion of the adrenal and x ray therapy to the pituitary a definite improvement in the patient's condition has been noted.

There is evidence in the literature and in this case that the fuchsinophilic staining reaction often referred to as the androgenic zone bears a direct correlation to the degree of masculinization in the female. However no claim is made that this staining reaction representing a hyperplasia of the androgenic zone is the only etiologic factor in the case. The possibility that these fuchsinophilic cells may be a by product of some other vital process as well as the role of the pituitary must still be considered.

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RADICAL PANCREATODUODENECTOMY WITH RESECTION OF THE PATENT PORTAL VEIN

AN EXPERIMENTAL STUDY

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TUMORS in and about the head of the pancreas yet stand as a challenge to the surgeon. These lesions usually produce symptoms early and thus should be most favorable for surgical treatment. This is not the case. Great strides have been made in our attack on this problem but a cure of carcinoma of the head of the pancreas remains a rarity. The reason for this seeming paradox lies in the anatomic relationship of the structures in this area, chief among which is the close proximity of the portal vein to the intrapancreatic portion of the common bile duct. Although these tumors when small in size involve the bile duct producing obstructive jaundice even this early they have usually likewise involved the pancreatic tissue about the portal vein if not the vein wall itself. The surgeon approaching such a tumor is beset by a problem which uncommonly can be solved by existing methods. If his technique is radical enough to remove the tumor adequately he is likely to damage vital blood vessels. On the other hand cautious sparing of these structures too often leads to incomplete removal of tumor tissue. It seemed to us that adequate treatment of these lesions necessitates resection of the portal vein.

It has long since been shown that neither the duodenum nor the head of the pancreas is necessary for maintenance of life. As early as 1877 von Eck had successfully performed his later famous Eck's fistula in dogs.¹ He was able to ligate the portal vein and anastomose it to the vena cava with survival of the animals. Many variations of his technique have been used both experimentally and clinically. Whipple² and Blakemore³ have recently reported the successful use of a vitallium tube in anastomosis of the portal vein to the vena cava in the treatment of portal hypertension. Thus both experimental and clinical investigations indicate that the portal vein need no longer be considered vital if its blood be shunted into the systemic venous circulation. We have been studying the possibility of combining the present day techniques of pancreatoduodenectomy with portal vein resection the continuity of the venous return from the bowel being reestablished by the use of a superior mesenteric vena caval shunt.

METHOD

First, six healthy adult dogs were subjected to portal vein ligation with implantation of its distal cut end into the vena cava immediately above the renal veins. The dogs were anesthetized with intraperitoneal injection of sodium

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TABLE I RESULTS OF OPERATIONS

DOG NO				COMMENT	weight gain tent without
353					
454	Nembutal	None	140 days	thrombosis	
350	Nembutal	None	129 days		
406	Nembutal	None	1 day	bowel in cava Inadequate postoperative care vessel anastomosis patent without thrombosis	
473	Nembutal	None	12 days	Sacrificed because of persistent vomiting Had an ileocolic and an ileo-cecal in tu anastomosis patent without thrombosis	
601	Nembutal	None	3 days	Generalized peritonitis bowel normal anastomosis patent without thrombosis	
					had malperfora anastomosis
592	Nembutal	None	12 hr	Died without recovery from anesthetic Hepatic artery ligated vessel anastomosis patent without thrombosis	
526	Nembutal	None	1 day	Died without recovery from anesthetic vessel anastomosis patent without thrombosis	
202	Nembutal	None	2 hr	Died in shock with marked blood loss into stomach and spleen after ligation of the splenic vein anastomosis patent without thrombosis	
492	Nembutal	None	0	Died before completion of operation	
460	Nembutal	None	3 hr	Died with ut recovery from anesthetic vessel anastomosis patent without thrombosis	
490	Nembutal	None	0	Died before completion of operation	
430	Nembutal	400 cc whole blood	0	Died immediately after operation vessel anastomosis patent without thrombosis	
448	Ether	200 cc whole blood	1 day	Died after convulsions vessel anastomosis patent without thrombosis no gross	
558	Ether	None	7 hr		
461	Ether	None	2 days		
381	Ether	None	4 hr		
597	Ether	600 cc whole blood	81 days	bowel Died after terminal weight loss had four jejunal ulcers vessel anastomosis pat ent without thrombosis	
644	Ether	400 cc whole blood	1 day	Died aspiration bronchopneumonia ob struction of cholecystojejunostomy vessel anastomosis patent without thrombosis	
598	Ether	200 cc whole blood	1 day	Died bronchopneumonia bile peritonitis from cholecystojejunostomy leak ves sel anastomosis patent without throm bosis	

TABLE I—CONT'D

DOG NO	ANESTHESIA	TRANSFUSION	SURVIVAL	COMMENT
468	Ether	300 cc Whole blood	1 day	Died early peritonitis from cholecystojejunostomy leak vessel anastomosis patent without thrombosis
443	Ether	300 cc Whole blood	" days	Died distemper animal refused to eat and had distemper vessel anastomosis patent without thrombosis
70	Ether	250 cc Whole blood	3 days	Died early peritonitis obstruction of cholecystojejunostomy cholangitis with liver abscesses vessel anastomosis patent without thrombosis
587	Ether	200 cc Whole blood	2 days	Died at operation dog had advanced cirrhosis of liver vessel anastomosis patent without thrombosis
399	Filter	150 cc Whole blood	1 day	Died distemper and generalized peritonitis bowel normal vessel anastomosis patent without thrombosis
573	Filter	None	1 st hr	Died in shock vessel anastomosis patent without thrombosis
544	Ether	600 cc Whole blood	34 days	Died perforated jejunal ulcer with peritonitis vessel anastomosis patent without thrombosis

pentobarbital 0.32 Gm per kilogram of body weight. The abdomen was entered through a long right rectus incision and the intestines were reflected to the left. The superior mesenteric, splenic and portal veins were freed by sharp dissection from the surrounding tissues. The superior pancreaticoduodenal vein was identified, ligated and divided. The vena cava and renal veins were similarly mobilized. A rubber shod umbilical cord clamp was then applied to the origin of the portal vein after which the vein was ligated flush with the liver and divided below this ligature. A Blakemore and Lord tube of appropriate size was ligated on the free end of the portal vein according to their technique.⁴ A segment of vena cava was then isolated by application of clamps to the renal veins and to the cava above and below the site of implantation. A defect was made in the anterior wall of the isolated cava within the circle of two previously placed purse string sutures. The portal vein covered vitalium tube was inserted into the caval aperture and anchored by ligation of these sutures.

Next twenty-two healthy adult dogs were subjected to the radical combined operation. In this procedure the major part of the pancreas together with the duodenum and the lower fifth of the stomach was resected. The distal cut end of the duodenum was infolded with purse string sutures and the common duct ligated and divided. An end-to-side gastrojejunostomy was established following which the portal vein was ligated, divided and implanted into the cava as outlined previously. A cholecystojejunostomy was constructed and the abdomen closed without drainage. Sodium pentobarbital anesthesia was used in the first eight animals and ether in the remaining fourteen. All animals were given intravenous infusions of saline solution during the operation and in addition the last eleven dogs received whole blood in amounts varying from 150 to 600 cc. Postoperatively animals which survived more than a few hours received parenteral saline and dextrose solutions. All animals were given postoperative injections of sodium penicillin 10,000 units every five to six hours.

RESULTS

The results of these operations are summarized in Table I

The anastomosis remained patent without thrombosis in all six of the animals with a simple portal caval shunt. Three of these animals survived for long periods and were sacrificed. One died in the first postoperative day, apparently from lack of adequate postoperative care. One died on the fifth postoperative day and at autopsy was found to have an extensive suppurative



Fig 1—Multiple stomal ulcerations found at autopsy of Dog 45* forty-seven days after operation

and at autopsy was found to have a complicated abscess which resulted in intestinal obstruction

The first eight dogs subjected to combined pancreatoduodenectomy and portal caval shunt were anesthetized by intraperitoneal injections of sodium pento-

barbital Of this group seven died within the first twenty four hours after operation without regaining consciousness The remaining dog lived for forty-seven days

The last fourteen dogs received ether by inhalation The first four animals of this group regained consciousness but all died within the first forty-eight hours, one with occlusion of the hepatic artery, one as the result of kinking of the superior mesenteric vein, one with cholangitis and liver abscesses, and one following a series of convulsions Nine of the remaining ten dogs were transfused with whole blood during operation Seven of these animals received an average of 300 cc of whole blood but all died during the first week, three as the result of extensive bronchopneumonia two with distemper, one with obstruction of the cholecystojejunostomy stoma, and one because of previous liver disease Two dogs of this last group received 600 cc of blood each and each made an uneventful recovery from the operation living for thirty four and eighty four days respectively

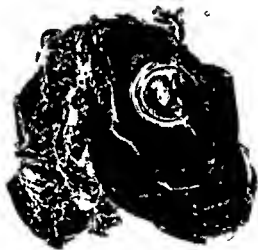


Fig 2—Appearance of anastomosis in Dog 59 eighty four days after operation. The posterior wall of the vena cava has been incised to expose the well healed anastomosis in its anterior wall The lumen of the superior mesenteric vein appears much reduced because of lack of attachment

Each of the three long surviving dogs developed stomal ulcerations and died as a result of this complication (Fig 1) Two developed frank perforation with generalized peritonitis and the third died after a period of persistent vomiting marked dehydration and emaciation Obstruction of the portal caval shunt occurred in only one animal in the entire series and this resulted from kinking of the mesenteric vein The remainder of the vessel anastomoses healed

cleanly and remained patent (Fig 2). The one exception to this was the single occurrence of a small mural thrombus which produced no obstruction of the vena cava.

COMMENT

Surprisingly enough anastomoses of the portal vein to the vena cava caused relatively few early local or general complications and the few which did occur were directly traceable to faulty technique. Apparently sufficient impairment of hepatic function occurs to make barbiturate anesthetics contraindicated in this work. Ether proved to be a satisfactory anesthetic agent. That blood loss into the visceral circulation during portal vein occlusion and into the inferior systemic circulation during caval occlusion is of considerable amount is borne out by the necessity for transfusion of large volumes of whole blood. In all probability a few animals could have been salvaged by more adequate postoperative care although blood transfusions during operation seemed to be the most important single factor influencing survival. The fact that all three of the dogs which survived for a considerable period had extensive gastrojejunal ulcerations would seem to indicate the need for more extensive gastrectomy or vagotomy as part of the procedure.

The results observed in these animals although disheartening are yet promising enough to warrant further investigation. The most important factors in successful instances seem to have been careful surgical technique, adequate whole blood transfusion during operation, and careful postoperative care.

CONCLUSIONS

A radical pancreateoduodenectomy with portal vein resection has been shown to be possible in the dog. Its complications have been tabulated.

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A METHOD OF CRANIOPLASTY USING READY MADE ACRYLIC CRANIOPROSTHESES

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METHYL methacrylate is a synthetic thermoplastic compound well known to the plastics industry and to aircraft manufacturers as Plexiglas, Lucite, Perspex, Acryloid or simply Acrylic or Acrylic Resin. It is less well recognized as a cranioplastic material although it antedates the currently popular tantalum for this purpose.

The usual methods of shaping either tantalum or acrylic into cranioprostheses are fundamentally identical and depend on dental impression techniques. A ready made method of cranioplasty was developed for tantalum¹ to obviate such lengthy and comparatively elaborate procedures. Intermediate preparatory craniotomies and laboratory processing. This proved so satisfactory in a variety of unpredictable situations that acrylic was substituted for the metal combining the merits of the method with those of what promises to be a superior cranioplastic material.

An acrylic hemisphere of fixed radius is formed by pressure molding the easily obtained acrylic sheet stock. This serves as a basic exemplar whose radius is identical with that of the four major spheroidal surfaces of the skull all of which possess practically equal radii of curvature.¹² This method of cranioplasty thus simply and directly replaces one spheroidal surface (the area of the bony defect) with a basically identical one of transparent plastic. Fig. 1 illustrates the very near duplication of the major skull contours by merely placing a segment of a basic acrylic prosthesis in various positions on a skull. One of these bases is routinely sterilized for all cranial operations and provides one or more specific prostheses depending on the size of the cranial defect.

This method of cranioplasty is applicable regardless of the extent and location of a skull defect whether it be of a complex fronto-orbital type or of a simple parietal variety (Fig. 2). No special instruments or tools are required and but a single item of easily constructed homemade equipment is necessary for shaping the plastic. The procedure for forming a basic cranioprosthesis and the details of its use are described in the paragraphs that follow.

LITERATURE

This remarkable plastic is available as either a molding powder or as commercially cast sheet stock of almost any desired thickness. Both forms of the substance have been used for cranioplasty.

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The opinions or assertions contained herein are the private ones of the author and are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large.

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First utilized for cranial windows in experimental rabbits because of its unique optical properties¹⁰ Zander was the first to use acrylic in human cranioplasty, in October, 1940. The prosthesis for the large left frontal defect in his one case was form molded over a plaster replica of the wanting bone.¹⁰

Walker and his group (Taggart, Lambros and Woolf) began using acrylic for human cranioplasty in 1941^{7, 11, 12} and followed the form molding technique after first processing their own plastic plates. Gurdjian, Webster and Brown essentially duplicated Zander's technique in their case the next year⁴ and Kahn also employed it in four of his cases but failed to mention the method used.¹

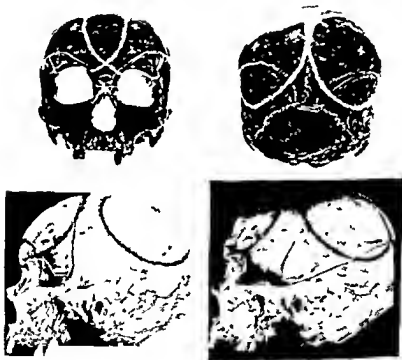


Fig 1—Conformity of a half segment of a basic acrylic cranioprosthesis variously positioned on a skull showing the four major spheroidal surfaces of equal radii.

Subsequently Walker and associates developed a denture construction technique in which a mold and counter mold of a defect are obtained through the

parent tailor made cranioprosthesis as employed by him in seven cases.²

In 1945 Small and Graham reported twenty five cases of acrylic cranioplasty in which they followed a modification of Walker's denture technique.¹³ The molds of a cranial defect were made directly at a preparatory craniotomy then after processing in the laboratory the prosthesis was inserted at a second

operation. This technique is also described in the recent paper by Elkins and Cameron on the work begun by J. M. Cameron and totaling seventy cases.² Independently, both groups of surgeons have shortened the laboratory processing time of the plastic to the extent that their technique is now a lengthy but one stage procedure. The original two stage method has been successfully applied to the production of entire acrylic calvaria for experimental monkeys by Sheldon Pudenz, Restarski and Craig.¹⁴

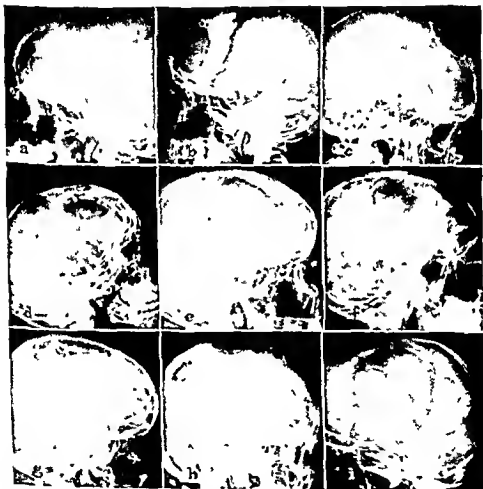


FIG. 2.—Postoperative roentgenograms. The position of the radiopaque acrylic in the defects is marked by the tantalum ribbon anchorings. a and b Fronto-orbital prostheses. c, d and e Frontal prostheses. f, g and h parietal and frontoparietal prostheses. i large frontotemporoparietal prosthesis.

These comparatively elaborate technical methods are all productive of accurate cranioprostheses but lack the very obvious advantages of equally, or more accurate ready made methods as designed for vitallium,¹ tantalum,¹² and now for acrylic cranioplasty.

PRESSURE MOLDING EQUIPMENT

One of the most spectacular physical properties of methyl methacrylate is its elastic memory—the material permits molding into almost any shape when heated reverting back to its initial conformation when reheated.¹² In common with all other thermoplastics acrylic experiences a physical change only when heated to its molding temperature.¹³ These propensities allow this material to be shaped by one or more of three different molding processes (1) pressure molding (blowing) (2) vacuum molding or (3) form molding. All of the cranioprotheses employed in this present series of seventeen cases were formed by the pressure (blow)—molding method. After extensive experimentation the prostheses produced in this manner consistently proved to be the most perfect the most easily and most rapidly formed.



FIG. 3—Pressure molding unit. a Unit closed for carrying. b Unit open and ready for molding (heating unit opened to show insertion of acrylic between incandescent globes). c The blowing unit containing a newly formed bubble contacting the horizontal thread and showing the pressure line and valve.

A pressure molding unit may be assembled in a few hours and, like my series and sheets of acrylic

The heating unit (Fig. 3 b) may be any device for developing a temperature of about 275° F whether this be ordinary incandescent or infrared globes the kitchen oven a Bunsen burner or heating elements. By and large oven type heating is the most satisfactory and four 100 watt globes, so arranged that the sheet plastic can be suspended between them provides adequate and even heating

The blowing unit (Fig 3, b and c) is simply a flat surface (forming table) containing a countersunk pressure outlet a template (forming ring) and an adequate clamping device. The template is plyboard with a cutout circular center of $2\frac{1}{2}$ inch radius centered over the pressure outlet in the forming table. Four fixed bolts with wing nuts securely batten the template and heated acrylic down to this surface. Flannelette (or thin felt) is used to cover the forming table (and the attached working table) to prevent blemishes in the heat softened acrylic as any defect in a contacting surface however infinitesimal is assuredly transferred to the material. This plastic duplicates a surface whether a defect or a polish. Likewise the use of flannelette mittens spares both the plastic and the hands.

A thread tightly stretched between two upright posts and across the pressure outlet at a height of $2\frac{1}{2}$ inches (Fig 3 c) gauges the vertical radius of a prosthesis during its molding. This radius equals that of the template. Although the major skull prominences possess a common radius of $2\frac{1}{4}$ inches¹² within negligible differences the thickness of the plastic and the mechanical discrepancies in forming it necessitates this slight increase in radius to produce a basic prosthesis of the proper mensuration.

Carboys of carbogen oxygen carbon dioxide or compressed air provide adequate pressure. About 100 pounds of pressure per square inch is ideal and a small hand valve inserted in the pressure line offers instant control. Automobile fuel line tubing and fittings suffice where metal parts are used. Rubber pressure tubing from the carboy to the valve obviates a blowout and threaded (or wired) unions prevent slipped connections.

In actual production this equipment yields a basic chemoprosthesis every four minutes so that a long time supply can be molded in the course of one or two hours. Also by varying the size and shape of the template opening the acrylic can be molded into divers forms serving many purposes so that the molding unit does possess some versatility.

PRESSURE MOLDING TECHNIQUE

Commercially cast sheets of acrylic (said to be more chemically inert than that processed from molding powder⁶) are marketed in practically any thickness. The $3/32$ inch sheet is the most satisfactory for the purpose at hand retaining a thickness of about 1.5 mm after molding. Sheets of $2/32$ or $4/32$ inch thickness may be used if thinner or thicker prostheses are desired. This material is readily obtained at low cost in hobby marts and most novelty shops.

A 6 by 6 inch square of sheet acrylic is suspended in the heating unit after removing the protective adhesive paper from both of its surfaces. It quickly acquires a wobbly flexibility and is then rapidly placed on the forming table and secured under the template. As the pressure valve is slowly opened the heated plastic expands into a bubble or blister (Fig 3 c). When its summit contacts the horizontal thread the flow of gas is reduced enough merely to maintain contact between the two until the material cools.

PRESSURE MOLDING EQUIPMENT

One of the most spectacular physical properties of methyl methacrylate is its elastic memory—the material permits molding into almost any shape when heated reverting back to its initial conformation when reheated.¹³ In common with all other thermoplastics acrylic experiences a physical change only when heated to its molding temperature.¹⁴ These propensities allow this material to be shaped by one or more of three different molding processes (1) pressure molding (blowing) (2) vacuum molding or (3) form molding. All of the cranioprostheses employed in this present series of seventeen cases were formed by the pressure (blow)—molding method. After extensive experimentation the prostheses produced in this manner consistently proved to be the most perfect the most easily and most rapidly formed.



Fig 3—Pressure molding unit. a Unit closed for casting. b unit open and ready for molding (heating unit opened to show insertion of acrylic between incandescent globes). c the blowing unit containing a newly formed bubble contacting the horizontal thread and showing the pressure gauge and valve.

A pressure molding unit may be assembled in a few hours and like my original crude and unfinished equipment need not be as elaborate as the portable bubble box illustrated in Fig 3 a. A heating unit and a blowing unit are conveniently combined in a plywood box with ample carrying space for accessories and sheets of acrylic.

The heating unit (Fig 3 b) may be any device for developing a temperature of about 270° F whether this be ordinary incandescent or infrared globes, the kitchen oven, a Bunsen burner or heating elements. B₁ and large oven type heating is the most satisfactory and four 100 watt globes so arranged that the sheet plastic can be suspended between them provides adequate and even heating.

TECHNIQUE OF CRANIOPLASTY

Each basic cranioprosthesis is thoroughly washed in warm, soapy water (not hot water) then sponged with ether and alcohol immediately prior to sterilization. This treatment removes any of the adhesive remaining on the plastic from its protective paper and permits sterilization by immersion in solutions. While sterilization in 1:1000 mercuric oxycyanide has averaged about two hours in my cases, a one hour treatment is probably sufficient.¹ A one hour exposure in 0.1 per cent mercuric chloride has been recommended² as well as twenty four hour immersion in 95 per cent alcohol³ or fifteen minute sterilization in Bard Parker solution.³ It is very important that the solution be agitated occasionally to disrupt air bells adhering to the surface of the plastic and a prosthesis must be thoroughly rinsed with sterile water or saline solution (not hot) before use. Autoclaving or boiling are impossible of course unless a suitable mold is made.

The edge of every bony defect is rongueured until viable bone is encountered whether a primary or a secondary repair is being performed or an onlay or inlay type of cranioprosthesis contemplated. In the usual case the surrounding bone is secure and tolerates the slight trauma of rabbeting which permits the more desirable inlay type of prosthesis (Fig 5 a and b). The rabbet (shelf mortise or rout) is formed with a $\frac{1}{4}$ inch shoulder and a depth corresponding to the thickness of the prosthesis. Any flat chisel will suffice although a rabbeting chisel facilitates this step.¹²

The operator can directly trace the margins of a bony defect with bone wax on a segment of a basic prosthesis placed over the area or a piece of lead foil (cottonoid will do) may be digitally crimped along the bony margin cut out and then outlined on the plastic (Fig 6). In either case the desired section of acrylic is removed and will be found to conform to the surrounding skull contours in all major respects.

Minor secondary adjustments and alterations are necessary only in the fronto-orbital areas or when a defect includes an area of both greater and lesser curvature. Acrylic lends itself well to manipulations of this kind. A basic cranioprosthesis supplies the fundamental over all curvature while an edge or corner of a cutout segment may be dipped in hot water (from the autoclave) and easily molded with the fingers as desired. A little experience renders this material almost as easily worked as modeling clay and one can readily duplicate missing contours such as an orbital plate or a supra-orbital ridge (Fig 2 a and b).

It may occasionally be desired to obliterate a dead space under a prosthesis or compensate some soft tissue deficit. Scraps of sterile acrylic are readily cemented to a prosthesis for this purpose with acrylic cement, acetone or glacial acetic acid.

Any of the nonabsorbible suture materials may be used to secure a prosthesis to the bone since acrylic is a nonmetal and there is therefore no electrochemical hazard. Cotton suture was employed in the first of my cases while tantalum ribbon anchorings were used in the remainder. Silk^{11, 14} and steel wire¹⁵ have been used and Sheldon and associates secured their lucite monkey

Basic prostheses formed in this manner suggest a transparent derby hat with a square brim (Fig 4). The crown is cut from the brim about $\frac{1}{4}$ inch above their junction. Several of these may be formed at one time and stored for future use without change in shape or chemical composition. The flat remnants may be salvaged for making acrylic cement.*

Any imperfect bubbles may be returned to the heating unit where the plastic will resume its initial flatness ('elastic memory') and can be molded again—there is thus no loss or waste. Too great too little and sudden blasts of pressure should be avoided. One should strive for even heating of the plastic remembering that suddenly liberated gases have a cooling effect—the material should be heated to the extent that it has the flexibility of moistened blotting paper before removing it from the oven.

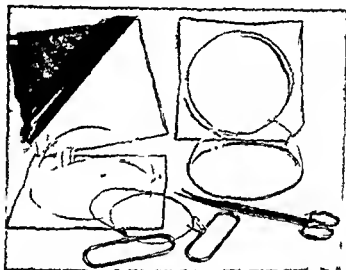


Fig 4—Sheet of acrylic, a newly formed bubble, and a completed basal prosthesis.

Although the forming equipment is inexpensive and simple of construction and operation commercially produced basic cranioprostheses would add little to the cost but something to convenience should this ready-made method of cranioplasty find favor. The acrylic arthroplasty cups used by some orthopedic surgeons are provided in this manner.*

Despite a soft surface acrylic is a rugged and tough substance which in the thickness used for cranioplasty has working qualities comparable to lead. A Gigh saw or curved dissecting scissors readily cuts a prosthesis (Fig 4) as will the actual cautery although the characteristic acetic odor evolved may be objectionable. Motor driven saws and router type instruments common to neurosurgical and orthopedic operating rooms work this plastic admirably. A small hand drill suffices for forming holes in the material.

*Acrylic shavings dissolved in ethylene dichloride or in acetone form an excellent cement for welding pieces of plastic together for impregnating cotton or silk sutures and for liquid adhesive in applying small dressings.

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calvaria with tantalum or vitallium screws¹⁴ Tantalum wire would also serve although tending to bite into the plastic when tightly cinched Some depend solely on pericranium sutured over a prosthesis to retain it in position¹⁵ Should the surgeon prefer to employ plastic materials throughout either plastigut¹⁶ or nylon suture may be used



FIG. 3.—A skull defect and an inlay type acrylic prosthesis. a The defect rabbit and prepared for the prosthesis. b the acrylic inlay anchored in place with tantalum ribbons. (a length of rubber dam was placed under the plastic to accentuate the photograph)

Both the onlay and the inlay types of prostheses are anchored in the same manner via matched holes in the prosthesis and through one or both tables of the skull. Two to four pairs of holes are ordinarily sufficient. The suture material is threaded through each pair and then tied or twisted. Once a prosthesis is firmly fixed in position the cut ends are bent upon themselves and turned down into the holes in the bone (Figs 2 a and c and 5 b). A prosthesis should never be forced to fit even though it is reasonably flexible—the plastic should always conform to the defect to avoid needless stress on both the material and the bone.

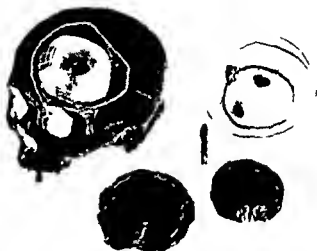


Fig 6—A defect may be traced directly on a segment of a basic prosthesis with bone wax or a lead foil pattern may be made and similarly outlined.

The scalp is sutured in the usual manner after suturing the pericranium if a sufficient amount of this structure remains. A single Penrose drain is routinely placed in a dependent position under the scalp and is not removed until the third or fourth postoperative day thereby obviating fluid collections.

Neither sulfa drugs nor penicillin have been applied locally during closure as a routine practice.^{8, 12} Neither have any of the cranioprostheses used in my cases been perforated to allow egress of fluid or to coax granulations from the scalp, this being proved unnecessary in work with tantalum.²

The routine head dressing consists of quantities of well fluffed sterile gauze under two snugly applied elastic bandages. Except for the one removal necessary for extraction of a drain the wounds are not dressed until time to remove the sutures.

MATERIAL

This method of ready made acrylic cranioplasty has been employed 18 times in 17 patients (one patient, Case 4, harbored two defects) since Jan 11 1946. The regional distribution included 4 fronto-orbital, 3 frontal, 7 parietal and 4 fronto-temporoparietal defects (Fig 2). Eight of the cases were compound comminuted fractures repaired in six hours, one three and four months

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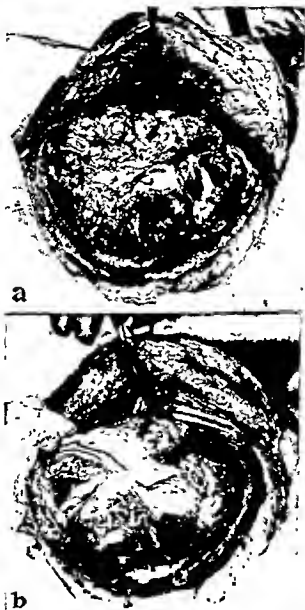


FIG 5—A skull defect and an inlay type acrylic prosthesis. a The defect rabbeted and prepared for the prosthesis. b The acrylic inlay anchored in place with tantalum ribbons (a length of rubber dam was placed under the plastic to accentuate the photograph)

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and two, three, four, and nine years after injury, 5 cases were skull tumors repaired primarily, 3 cases were operative defects resultant from sacrifice of a bone flap, and 1 case was a rapidly enlarging frontal pneumocephalus dilatans. All received the inlay type prosthesis.

In no instance was cranioplasty the major indication for operation. The clinical aspects of these cases and the merits of acrylic are considered in a second paper now under preparation, however.

RESULTS

In general the use of acrylic made cranioplasty an appreciably faster and easier procedure than when employing tantalum. The ready made method proved satisfactory and the repairs were accepted as technically and esthetically gratifying in each case. The one fatality was not attributable in any way to either the cranioplasty, the material or the method. Convalescence proceeded uneventfully in the remaining cases and the scalp was firmly adherent to the prosthesis within a period of two weeks.

SUMMARY

- 1 The rationale, procedure for forming and method of using a ready made acrylic cranioprosthesis are described.
- 2 The technique of fashioning and inserting onlay and inlay types of prostheses is presented.
- 3 The major technical virtues of acrylic for cranioplasty are
 - (a) Its thermoplasticity allows easy and rapid molding and secondary alteration of basic cranioprostheses.
 - (b) The characteristic transparency permits accurate visual tracing of skull defects with bone wax.
 - (c) It is readily worked with ordinary instruments.
 - (d) Its cementing facility provides for plastic replacement of soft tissue and the obliteration of dead spaces.
- 4 Economically acrylic is readily obtained at extremely low cost.

CONCLUSIONS

- 1 The principal advantages of the ready made method are
 - (a) A ready made acrylic prosthesis is instantly available at all cranial operations.
 - (b) Accurate replacements of any cranial defect are easily and quickly effected.
 - (c) Intermediate preparatory craniotomies are avoided.
 - (d) The surgeon is independent of lengthy processing techniques special equipment technicians and hospitals providing them.
- 2 Both the method and the material have proved technically and esthetically satisfactory in a series of seventeen patients harboring cranial defects such as those encountered in civil neurosurgical practice.

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CONDYLAR GROWTH AND MANDIBULAR DEFORMITIES

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THIS report is an analysis of nineteen cases of arrested growth in the mandibular condyles. It is the purpose of this study to emphasize the importance of this area in the development of the jaw as well as in its function.

Mandibular growth results from an integration of activities in a number of areas. Surface apposition particularly at the alveolar margin posterior border of the ramus, coronoid tip and epiphyseal like growth at the condyle are responsible for major contributions. Concurrently, there is continuous surface remodeling. Normal development of the mandible depends upon synchronous coordination of the growth activities of the various centers. Interference with any one of them may be expected to alter the orderly progression of development. Thus growth arrests in the condyles reflect themselves as pronounced mandibular deformities.

The histology of the area has been described by Toldt¹ Sicher² Charles³ and more recently again by Sicher and Weinman⁴ Rushton⁵ and others. This center appears in the 30 mm stage of the embryo and its activity attains peak levels during the prenatal period.

Microscopic examination (Figs 1, 2 and 3) reveals the presence of three zones: (1) chondrogenic, (2) cartilaginous, (3) osseous. The condyle is capped by a narrow layer of fibrous tissue which contains connective tissue cells and a few cartilage cells. The inner layer of this covering is chondrogenic giving rise to hyaline cartilage cells which constitute the second zone. There is interstitial proliferation of the cartilage and in the third zone one observes ossification occurring around the cartilage scaffolding. The picture is analogous to that observed in the endochondral epiphyseal ossification of a long bone.

The condylar growth center maintains its activity longer than most other centers in the head persisting until at least the twentieth year. This provides the forward and downward vector for mandibular growth and contributes as well to increased width of the jaw.

Examination of the condyle in gross specimens taken from *Macaca rhesus* monkeys which had received injections of alizarin red revealed deep staining indicative of intensive growth activity. Cephalometric studies tended to confirm these findings.⁶

Disturbance of this area is not uncommon.^{7, 8, 9, 10, 11} It may occur as one of the sequelae of a mastoiditis or middle ear infection. Hematogenous¹²

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infections or those which spread from the dental area may localize in the joint and lead to interference with chondral activity or to ankylosis and/or functional limitations. Similar effects sometimes proceed from traumatic injuries resulting in fractures or in disturbance of the bone forming cartilage. Two of our cases of arrest were associated with a generalized arthritis which had also involved the temporomandibular joint. In deformities in such cases have been reported by Dimmonberger (1891), and Ibrahim (1914).¹² More rarely inactivation of growth results from neoplasms or congenital absence of structure.¹³ Endocrine disturbances in animals have been shown to effect condylar growth.¹⁴ An excellent review of the whole subject has been prepared by Rushton.¹⁵

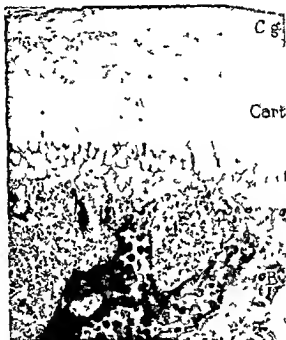


Fig. 1—Temporomandibular joint area of condylar cartilage. Note the three layers: (C) cartilage, (B) bone, and (Cg) chondrogenic zone.

In a study of normal and abnormal facial growth patterns, one of us reported three cases of injury to the condylar center that were analyzed using the technique of Brodient.² (Two of these are included here with further records.) The significance of such disturbances in the production of facial asymmetry was shown by Thompson.¹⁶ (See cases J G and R M in this report.)

MATERIAL AND METHOD

A series of nineteen cases with history of involvement of the condyle was studied (Table I). Injury of the condyle was determined on the basis

SUMMARY OF DATA IN NINETEEN CASES OF CONDYLOMA CROCODATI

[illegible]

J A	Shortly after birth or congenital	Otitis at 10 with surgical intervention	Left	Untreated	None	Middle line deviated to left on opening, left external pterygoid involved, no right lateral excursion	Unilateral deviation of left ear canal, middle skewed to left, unilateral notching
I I	Unknown	Unknown	Right	Untreated	None	Opening somewhat limited, middle deviated to right on opening, no left lateral function, right external pterygoid involved	Mandibular left lateral teeth in lingual occlusion, mandible skewed to right unilateral notching
I G	1 1/2 yr	Ankylosis following infection	Left	Treated	Arthroplasty at 1 1/2 yr	Opening increased following surgery, middle to left on opening, no right lateral function, left external pterygoid involved	Mandible skewed to left, unilateral notching
I M	Unknown	Unknown	Left	Untreated	None	Middle line deviated to left on opening, no right lateral function, left external pterygoid involved	Lower middle skewed to left, unilateral notching
II G	2 yr	Infection and possible otitis	Left	Treated	None	Middle line deviated to right on opening, no left lateral function, right external pterygoid involved	Marked skewing of mandible to left unilateral notching
II M	1 1/2 yr	Involvement of frontoenteral segment to infection	Right	Untreated	None	Middle line deviated to right on opening, no left lateral function, right external pterygoid involved	Skewing to right unilateral notching
II K	Congenital at 2 yr	Ankylosis subsequent to birth injury	Left	Untreated	Arthroplasty at 3 11 16 yr	Middle line deviated to right on opening, no left lateral function, right external pterygoid involved	Lower right lateral segment lingual to upper mandibular left buccal segment buccal to upper 2 cm opening unilateral notching
F C	8 to 9 yr	Ankylosis subsequent to dental infection which developed into septicaemia and localized in the ten paramandibular joint	Right	Treated	Arthroplasty 14 1/2 yr	Middle line deviated to right on opening, no left lateral function, right external pterygoid involved	Unilateral notching
J B	14 to 15 yr	Recurrent mastoiditis which was operated at 10 10 yr	Left	Treated	None	Middle line right lateral excursion possible left external pterygoid involvement	Slight skewing of mandible to left, mandibular left segment in lingual occlusion, no notch

of (1) history, (2) roentgenographs of the area (cephalometric, lamina graphic, and routine temporomandibular films), and (3) analysis of joint function

The roentgenographic technique used (Broadbent Bolton cephalometer) insured consistency of results and the standardization permitted superposition of subsequent film tracings.² Laminagraphic and routine roentgenograms of the temporomandibular joint were made in a number of cases

In eight instances it was possible to follow the same individual serially over periods ranging from one to twelve years. In eight cases the involve



Fig. 2.—Temporomandibular joint area of adolescent (Orban's). C = Chondrogenic zone. Ca = cartilage zone. B = bone.



Fig. 3.—Temporomandibular joint area of adult. Note the absence of the zone of proliferating cartilage (Orban's). A = articular eminence. Ad = articular disc. Cond = condyle.

ment was bilateral. The histories were unfortunately incomplete in many instances. Most of the individuals gave a history of a growth arrest that was early or congenital in origin. In others it was frequently associated with infections and subsequent ankylosis. However, significant functional impairment was not universally present. Orthodontic treatment was attempted in eight cases, six patients had arthroplasties.

For purposes of comparison the tracings of the mandibles of the same individual were superposed using the anterior portion and lower mandibular border as regions of relative stability since apposition and remodeling are minimal there. Measurements were made of the length of the lower



Fig 4

Fig 4—Photograph of D V illustrating the characteristic facial deformity occurring in a unilateral arrest. Note the flattening on the unaffected side (left) and the fullness of the right side.

Fig 5—Profile photograph of J P showing the characteristic facies found in bilateral condylar arrest.

border of the mandible as determined by the distance from gonion to gnathion. The angular relations between the lower border of the mandible and the sella nasion plane S N between the anterior part of the face (V Gn) and the sella nasion plane and between S Gu and the sella nasion plane were recorded (Table II Fig 15). These were compared with means determined from forty cases of excellent occlusion.*

CLINICAL FINDINGS

When there was unilateral involvement (Fig 4) the unaffected side usually appeared flat and underdeveloped while the arrested side of the face gave the impression of fullness. The mandible was skewed toward the side of the affected condyle. Palpation of the ramus body junction generally

TABLE II SUMMARY OF MEASUREMENTS

CASE	AGE		LENGTH OF LOWER BORDER OF MANDIBLE (GO GN)* (MM)	ANGLE OF LOWER BORDER OF MANDIBLE TO SN†	ANGLE D A L N	ANGLE A G GN
	YR	MO				
Control				32° 1' + 43°	41° 5' + 33°	() ° + 34°
A C	9	4	53	3	61	70
J F	10	11	4	39	61.5	9
I G	10	4	43	41	61	57
F W	1	4	51	6-3	61	83
	10	8	5			
	13	3	53			
	13	11	51			
	16	11	5			
	18	3	5			
V W	10	7	5	43	6	8
W U	13		53			
	14	11	53	50	64.5	83.0
	16	3	50			
	19	2	53			
	24	12	50			
N S	14	3	41	40	55	83
	15	3	40			
	17	2	43			
	18	2	47			
	19	0	47			
L R	21	9	56	54	63	81.0
P B		6	53	43	64.5	8
D S	8	8	44	25	64	
	9	7	44			
	10	1	43			
J A	10	8	51	53	60	8
J L	13	11	53		65	8
J G	14	9	63	40	64.5	83
	17	8	64			
	18	6	66			
J M	14	3	6	63	63	84
R G	15	7	61	50	66.5	80.0
R V	16	9	5	4	6	8
H K	1	4	53	50	63	8
	20					
F C	17	2	7	5	65	81
	19	7	53			
J B	19	11	53	5	63	8

*These measurements were made with correctional plates.

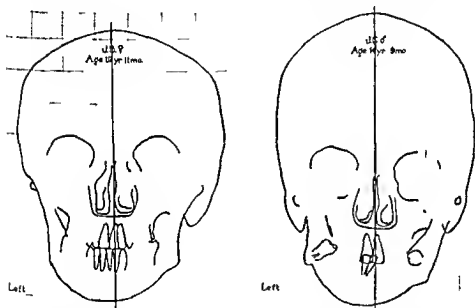
†The angle of the affected side was usually the mean of unilateral arrest. The mean between the two angles was utilized where there was bilateral involvement.

revealed notching of the lower border. The patient was frequently unable to deviate the jaw toward the normal side and the mandibular midline shifted toward the abnormal side on protrusion.

With bilateral arrest there was usually a symmetrical type of deformity (Fig 5). This resulted in a *Vogelbein* type with a markedly retruded mandible and with the chin lying in the buccal region. Lateral function was not always possible. Antegonial notching was present bilaterally in these cases.

ROENTGENOLOGIC FINDINGS

Cases Exhibiting Unilateral Arrests (Figs 6, 7, 8, and 9, Table I) — Comparison of the roentgenograms of J G with the history of arrest at $2\frac{1}{2}$ years with those of J B with an arrest occurring between 15 to 17 years illustrates two extremes of disturbed growth (Figs 6 and 7). In the latter instance the mandibular midline deviated to the affected side and there was a slight asymmetry in mandibular form. The S-N lower border angle was 38 degrees. There was a Class I malocclusion. In the case of the early arrest there was a marked skewing of the mandible toward the involved side. (In some instances this resulted in complete lingual occlusion of the mandibular teeth on the unaffected side.) The ramus was short and the



Figs 6 and 7—Tracings of frontal roentgenograms of two cases J B and J G superposed on ruler prior to indicate the relative distortion effect of late and early condylar arrests respectively. The left side was involved in both cases. (See Table I for history.)

body height was reduced. The lower border of the mandible just anterior to the junction of the ramus and body was notched and presented an abnormal convexity which was readily palpated. Superposition of the mandibular tracings of the retarded side (Fig 10) showed continued adherence to a distorted mode of growth over a period of four years. The S-N lower border angle was 45 degrees indicative of a failure of downward development.

The patient (J G) had a Class II malocclusion. (In the orthodontic treatment of this case the upper first bicuspids were extracted and the anterior teeth were retracted. Although there was some improvement in appearance the result was far from satisfactory.)

Arthroplasty in this patient, as in others seen by us did not restore the growth potential although there was improved function.

Cases Exhibiting Bilateral Arrests—Roentgenographic examination of those patients having a bilateral arrest (Figs 11 and 12 Table I) usually showed a symmetrical dysplasia.



Fig 8—Anteroposterior roentgenogram of D 5 showing characteristics of a unilateral condylar arrest. The right side was involved.



Fig 9—Lateral roentgenogram of D 5. Note notching of the right mandibular border.

Because of the failure in mandibular growth there is an elimination of the downward and forward movement which is typical of normal development. Apparently the downward component is disturbed more profoundly than the forward component. The evidence for this lies in the findings that the angle which may be constructed between the anterior cranial base S-N and the lower border of the mandible Go-Gn invariably lies outside the normal range (32° to 49°). Angles \angle S-Gn and \angle S-N-Gn also deviate markedly from the normal (Fig. 13 Table II).

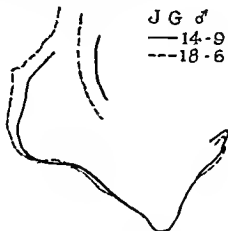


Fig. 10—Superposed serial tracings of the left side of the mandible of J. G. The growth pattern adheres to its dysplastic form.

Excellent serial data were available for three of the cases (W. U. F. W. N. S. Figs. 14, 15, and 16). The increment curves of the lower border of the mandible (Go-Gn) for the period of observation were plotted and compared to a control curve. In all instances there was considerable underdevelopment and a more rapid approach to asymptotic form than in the normal indicating a feeble growth potential which was never restored to healthy vigor. The dysplastic pattern was maintained and was unmodified by orthodontic treatment which was generally not successful. Certainly growth of the bone was not stimulated and the facial disharmony was accentuated by the opening of the bite which usually resulted from such treatment.

The case W. U. (Fig. 16) of this group is particularly interesting. Change in mandibular form was observed here and first reported by Brodie in 1941. The change to a dysplastic pattern occurred following bilateral condylar resection. The new form had then remained unaltered for ten years. The change in the growth curve was in reality not a measure of length change here but rather a reflection of the profound modification of mandibular form. Thus the mandible was actually not shortened but the location of the Go-Gn points had shifted.

Two of our eight cases of bilateral mandibular deformity developed as a result of polyarthritis in which the temporomandibular joint was also involved (J F, A G, Figs 5 and 11). They presented a picture which did not vary essentially from the characteristic bilateral condylar growth arrest.



Fig 11—Lateral roentgenogram of J F showing the characteristics observed in a bilateral condylar arrest. This was associated with a generalized arthritis.



Fig 12—Laminagraph of right temporomandibular joint of A G (generalized arthritis). The condyle is flattened and shortened characteristic of an arthritic process.

DISCUSSION

Disturbance of Growth—The problem of growth retardation resulting from a noxious influence on epiphyseal cartilage was reviewed by Kulms and

Swain in a paper on arthritis in children²² They cited the work of Vogt (1876) and Harris (1930) who pointed out that inflammatory processes or circulatory disturbances in proximity to an epiphysis may lead to disturbances in growth. The present paper deals with the effect of such influences on the active cartilage center at the head of the mandibular condyle. The cases reported illustrate strikingly the typical jaw deformity which results from the ensuing arrest.

When a premature ossification of epiphyseal cartilage occurs, as in chronic arthritis in children subsequent growth expectancy is poor. It appears that scarring and early ossification of the condyle head may occur not only in polyarthritis but following trauma or infection.

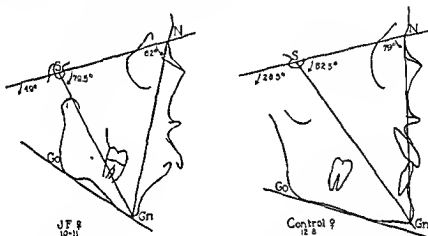


Fig. 13.—Tracings of facial patterns showing the differences in three significant angles noted between a normal child and one exhibiting a bilateral condylar arrest. The normal range is indicated in Table II.

The severity of the deformity is related to the chronology and duration of the arrest. In the case of a unilateral arrest an early disturbance leads to a marked facial asymmetry. Involvement in the period of growth regression leads to more subtle disturbances which may be reflected primarily by dental occlusal changes such as a shift in the mandibular midline without any profound change in mandibular size or form. This accounts for difference in the degree of distortion noted between J G and J B. Similarly the earlier bilateral arrests are associated with more pronounced deformities.

Sometimes the arrest is succeeded by a period of growth which is, however considerably decelerated. It is important to know something about the growth potentialities in these cases particularly where there is an ankylosis of the jaw. This may be deduced only from serial records over a period of two or three years. If the serial study indicates that growth activity is continuing, even at a low rate surgical intervention should be ruled out because such intervention will only superimpose another severe growth arrest as in the case of W U. If the cartilage has been prematurely ossified or

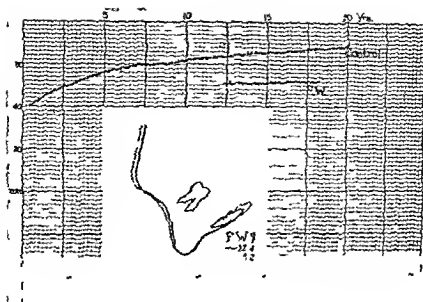


Fig. 11—Tracing of mandible of P W. Increment curve of lower border length (Ga, Ga) from 14 years 4 months to 18 years 4 months is plotted. A control curve has been developed from radiographic measurements. This has been extrapolated beyond the 8 year level. (Limited unpublished data tend to confirm the validity of the extrapolation.)

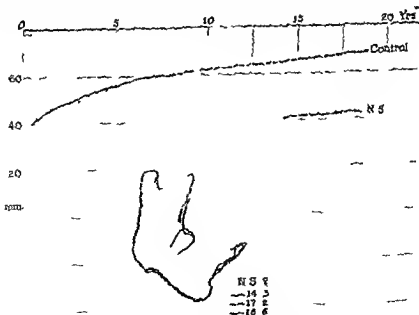


Fig. 12—Tracing of mandible of N S. Increment curve of lower border length (Ga, Ga) from 14 years 3 months to 14 years 6 months is plotted.

so badly scarred as to preclude further growth surgery is not contraindicated from the growth standpoint. In older individuals this does not constitute a problem.

The facial pattern in these cases of arrest lies outside the normal range (Fig 13), the deviation is uniform and characteristic and seems to be entirely a result of the mandibular deformity. The failure in forward development accounts for the acute angle $S \angle Gn$ and the more obtuse $\angle S Gn$. Failure in ramus height growth is reflected in the larger than normal $S \angle N$ mandibular border angle. This type of facial pattern is also seen in some extreme types of malocclusion (marked Class II Division 1 malocclusions). It is entirely possible that the etiology of such conditions may be traced to growth disturbances in the condylar center.

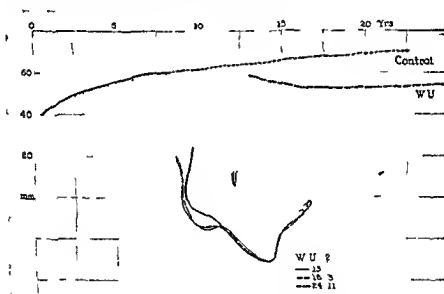


Fig 16—Tracings of mandible of W. U. Increment curve of lower border length (Go Gn) from 13 years to 24 years 11 months is plotted.

One may speculate upon the reason for the notching at the antegonion and the apparent distortion in mandibular form which are pathognomonic of the condylar growth arrest. The most satisfactory explanation would appear to be that growth continues at the angle of the mandible as a result of subperiosteal apposition. Because of the failure at the condyle forward and downward movement of the body does not occur, there is then a localized thickening of the bone at the angle which accentuates the antegonion. This coupled with the obtuse angle formed between the cranial base and the lower border of the mandible is responsible for the characteristic 'warping'.

Muscle imbalances have been regarded by some as the major factors involved in producing the dysplasia. The validity of such an assumption is difficult to sustain in view of the following findings:

1 Resections either of the condyle or horizontally through the superior portion of the ramus for the correction of mandibular prognathism were performed on an older group of patients (17 to 35 years of age). In none of these cases has there been any significant change in the form of body of the mandible over a subsequent period of several years.

2 Injury to the condylar area in the cases reported here was not always associated with muscle disturbance as evidenced by the normal range of functional movements in some.

3 The authors have seen cases of functional limitation of obscure etiology that is almost complete inability to open the mouth, where the condylar area was apparently undisturbed. In these individuals there was no deformity of the jaw.

4 This deformity does not occur in adult temporomandibular ankylosis.

Disturbance of Function—Condylar growth disturbances are frequently associated with limitations of function particularly the absence of lateral excursion on one side (Table I). This is readily understood if the dynamic anatomy of the external pterygoid is considered. This muscle which has two heads, lies in a horizontal plane running in a posterolateral direction from before backward. The superior head passes from the inferior part of the lateral surface of the great wing of the sphenoid and from the infratemporal crest, the inferior head originates on the lateral surface of the lateral pterygoid plate. The muscle inserts into the neck of the condyle and into the articular disc of the temporomandibular joint. The right muscle is therefore responsible for movement of the jaw to the left while the left muscle controls movement to the right. Both sides act together in executing protrusive and opening movements.

External pterygoid function was tested in our group of patients by having them execute these movements. Involvement of a muscle was indicated by (1) absence of contralateral excursion (2) deviation of the mandibular midline toward the affected side on opening (3) deviation of the midline toward the affected side on protrusion.

There is some evidence to indicate that the suprahyoids take over the major role of depressors of the mandible when both external pterygoids are inactivated.¹⁴

TREATMENT

The problem of treatment is a difficult one. There is no mechanism that will compensate for the lost or retarded growth. Although the deformity may not be progressive except in some cases of unilateral arrest it is not self-correcting, the dysplastic pattern of growth continues.

Since orthodontic treatment is capable only of modifying the alveolar process it is not effective in correcting the basic deformity. The orthodontist can only strive for a correction of the occlusal relations of the teeth. Even this is difficult because of the growth lag. It has been pointed out¹⁵ that the prognosis for successful orthodontic treatment of patients with facial patterns similar to those included here is poor. The reason may be similar

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ZIPPERED ELASTIC STOCKINGS

H D COGSWELL MD TUCSON, ARIZ

(From the Thomas Davis Clinic)

THE use of elastic stockings for the treatment of venous passive congestion and its complications (phlebitis, ulcers and eczema of varicosities) of the lower extremities is a generally accepted and valuable procedure.

With the aforementioned complications the application of an elastic stocking is painful, often causing loss of newly hard won epithelium in eczematoid or nearly healed ulcerations.



Fig 1



Fig 2

Fig 1—Application of gauze dressing at the site of a varicose ulcer. Overlying the gauze is a rubber sponge holding the dressing in place eliminating need for adhesive tape. This sponge also gives local pressure over the ulcer accelerating healing.

Fig 2—Zipper closed holding dressings in place. Muscular activity does not dislodge dressing.

By incorporating a zipper as illustrated the difficulty and pain in pulling on the elastic support are obviated. When applying dressings over a granulating area it has been found especially advantageous to use a zippered stocking as no adhesive tape is necessary, avoiding adhesive tape irritation and dressings may be easily changed (Figs 1 and 2).

The simplicity of sewing a zipper in place is demonstrated by the fact that in all instances the patient or a member of his family has sewn the zipper in the stockings.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK M.D.

III POST TRAUMATIC RENAL INSUFFICIENCY

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INTRODUCTION

THE importance and frequent occurrence of renal failure in that relatively small group of battle casualties who are seriously wounded must be emphasized. The present report describes (1) the clinical physiologic and biochemical features of this syndrome as we observed it and (2) the forms of treatment that were employed including certain therapeutic errors.

METHODS OF STUDY AND DIVISION OF CASES

Three main criteria have been utilized in grouping the patients who developed this complication. (1) The high azotemia group includes every patient who at some time during the period we observed him had a nonprotein nitrogen level of 65 mg. per cent or more. (2) The oliguria group includes patients with urinary output of 100 to 600 cc. for at least one twenty-four hour period. (3) The anuria group represents those patients with less than 100 cc. of urinary output for at least one twenty-four hour period.

Most of the cases in the high azotemia group are also included in either the oliguria or the anuria group (Table I). A large proportion of the cases in the oliguria and anuria groups fall of course into the high azotemia (Table II).

There is much overlapping in the three groups. Most of the averages however were obtained from the high azotemia group or portions thereof. Analysis of the anuria and oliguria groups in separate categories seemed desirable because a low urinary output provides a simple and useful means of recognizing such cases clinically.

Clinical Features

Mortality—The importance of uremia as a primary cause of death in all three groups is demonstrated in Table III. The cause of death was assigned

The Physiological Effects of Wounds
Wounded by the same authors (Gover)

*Director, Physiological Laboratory
†Now at Massachusetts General Hospital

TABLE I TYPES OF URINARY OUTPUT IN THE 'HIGH AZOTEMIA' GROUP

TYPES	NUMBER
Normal output	10
Oliguria	29
Anuria	27
Output unknown	7
Total cases	73

by clinical evaluation, blood chemistry and autopsy findings. Four of the five patients classified as 'no uremia or unknown' in the anuria group, died probably with at least coincident uremia. From these figures it is obvious that any patient who develops anuria by our definition has an extremely grave prognosis (30 patients, 91 per cent mortality in our series and 22 patients, 67 per cent in uremia). In the oliguria group while the mortality was high (21 patients, 47 per cent in the whole group) only 12 patients or 27 per cent died in uremia. In the 'high azotemia' group 30 patients or 69 per cent, died and 34 patients, or 47 per cent were in uremia.

TABLE II INCIDENCE OF HIGH AZOTEMIA IN THE ANURIA AND OLIGURIA GROUPS

	ANURIA	OLIGURIA
High azotemia	27	29
No azotemia	1	16
Nonprotein nitrogen unknown	3	0
Total cases	31	45

Degree of Initial Shock—Table III also shows the relationship between degree of initial shock and subsequent renal failure. If one excludes the crush cases, a true transfusion incompatibility and a case of sulfathiazole crystalluria in the no shock group, it becomes evident that there is a definite preponderance of renal failure in those who were recognized as having severe or moderate initial shock. Thus, if the exclusions mentioned are made 86 per cent of the azotemia group, 73 per cent of the oliguria group and 76 per cent of the anuria group had moderate or severe initial shock. Many patients may have had transient shock, even of several hours duration, before hospital entry but with no sign of

TABLE III TYPES OF DEATH AND DEGREE OF INITIAL SHOCK IN 'HIGH AZOTEMIA' OLIGURIA, AND ANURIA

GROUP	TOTAL	LIVED	DIED	TYPES OF DEATH				DEGREE OF INITIAL SHOCK					
				UREMIA	UREMIA CONTRIBUTING	UREMIA COINCIDENT	NO UREMIA OR UNKNOWN	TOTAL	NONE	SLIGHT	Moderate	SEVERE	UNKNOWN
High azotemia	31	—	30	14	—	13	0	73	6*	6	27	31	1
Oliguria	45	24	21	12	1	5	3	43	3	8	17	20	1
Anuria	30	3	20	22	1	12	5	31	8†	3	6	16	0

*Includes two crush cases, one transfusion incompatibility and one case with slight postoperative shock.
 †Includes one sulfathiazole crystalluria, one transfusion incompatibility and two crush cases.

this on entry. Our recorded figures are doubtless too low. However, it is not clear that the severity of the renal lesion is entirely determined by the degree of shock. Our series includes a few patients who so far as we could determine never had any marked degree of shock and yet developed subsequent renal insufficiency (Cases 22, 120, 138):

Role of Uremia as a Cause of Death, and Its Relationship to Time of Death After Wounding—The time of death after wounding in 51 patients with renal insufficiency is shown in Table IV. Of those in whom uremia was the primary cause of death, 41 per cent died in the first five days, 50 per cent in the second five days, or 91 per cent within ten days after wounding. Likewise, of all the patients, 94 per cent died within the first ten days. The significance of this time factor should be emphasized, for evidence will be presented that if the patients can be carried through this critical ten day period they stand a fair chance of recovery.

TABLE IV

TIME OF DEATH AFTER WOUNDING (DAYS)	ROLE OF UREMIA IN CAUSE OF DEATH (NUMBERS OF CASES)			
	PRIMARY	CONTRIBUTORY	COINCIDENT	UNKNOWN
1 to 5	11	2	8	0
6 to 10	17	1	3	0
11 to 14	2	0	0	0
Total	30	3	11	0

Types of Wounds—Types of wounds in the three groups of renal insufficiency are shown in Table V. In the "high azotemia" group peripheral wounds with fracture and intra abdominal wounds are of equal frequency. In the oliguria group peripheral wounds predominate whereas in the anuria group intra abdominal wounds are somewhat more frequent. Thoracic wounds rank third in all three groups. Wounds of the liver, kidneys and urinary tract occurred but not in high percentage in any group.

TABLE V. TYPES OF WOUNDS OR INJURIES IN PATIENTS WITH "HIGH AZOTEMIA," OLIGURIA AND ANURIA

TYPE OF WOUND	HIGH AZOTEMIA (NO. OF CASES)	OLIGURIA (NO. OF CASES)	ANURIA (NO. OF CASES)
Multiple major wounds	21	10	7
Single major wound	52	—	26
Peripheral with fracture	42	18	11
Intra abdominal	32	14	1
Thoracic	15	10	—
Peripheral without fracture	8	2	1
Thoracoabdominal	6	7	4
Liver	12	7	—
Kidney	10	—	1
Nephrectomy	6	4	4
Urinary tract, other than kidney	1	2	4
Crush cases	4	1	4
Burn	1	1	0
Spinal cord injury	2	1	0
Sulfathiazole crystalluria	0	0	1
Incompatible blood transfusion	1	0	1
Total cases included	73	45	37

Incidence of Hypertension Edema Eye Ground Change—Table VI indicates the number of patients in the high azotemia group who at some time in their course had a systolic blood pressure of 135 mm of mercury or higher or a diastolic of 90 mm or higher. These levels were decided upon as the probable upper limits of normal for the age group into which our patients fell. The hypertension was first recorded in the majority of patients within the first seven days after wounding injury or crush. In only 4 of the 71 were initial recordings made after that time. The probability is that even these patients had an unobserved hypertension prior to the first determination recorded. In general the pressure rose gradually reaching a maximum between the third and sixth days after wounding. This agrees essentially with the time of maximum nitrogen retention in the blood.

TABLE VI INCIDENCE OF HYPERTENSION IN HIGH AZOTEMIA

	TOTAL	HYPERTENSION (NO CASES)	NO HYPERTENSION (NO CASES)	HYPERTENSION (PER CENT)
Lived	7	13	13	13
Lived with minimal renal failure	1	3	7	40
Lived with recovery diuresis	11	10	0	100
Died	49	1	48	20
Died uremia primary cause	1	7	7	7
Died uremia contributory	3	1	2	25
Died uremia coincident	12	1	11	8
All cases	71*	44	7	12

*All cases are included in which adequate record of blood pressure was kept

Of the 20 patients who died but did not develop hypertension 13 died within the first four days after wounding 3 within six days and 4 within six to ten days. Many of these never really recovered from shock. Most of them possibly would have developed hypertension if they had lived longer especially the 7 patients in whom the primary cause of death was uremia.

Edema was clinically observed in 23 of the 73 cases in the high azotemia group. The degree varied but when present was usually generalized involving all extremities and the face. Eighteen instances were in patients who died. Three patients had generalized convulsions. Eye grounds were examined in 7 cases 3 showed abnormalities—flame shaped hemorrhages in 2 and a small exudate in 1. A pericardial friction rub was heard in one patient who died in uremia he showed pericarditis at necropsy.

LABORATORY METHODS

The laboratory methods are described in detail elsewhere.

BIOCHEMICAL ABNORMALITIES OF THE BLOOD AND URINE

In studying these patients who developed renal insufficiency we were dealing with a unique group of individuals. They were all normal men in a young age group and prior to wounding so far as known were physiologically sound. They had sustained severe wounds which almost at once produced changes in

their internal environment.^{1,2} The wounds and the changes produced were not severe enough considering the present effectiveness of resuscitation and other early treatment to cause early death. Largely because they were adequately treated preoperatively, they withstood operation fairly well, but beginning with the first day or two postoperatively (or after trauma if no surgery was done), they began to show clinical and laboratory evidence of inadequate renal function. The renal failure progressed rapidly, and in most instances the patients either died in uremia within the first ten days or later showed signs of beginning improvement of renal function (as shown by diuresis and clearance of nonprotein nitrogen) and subsequently recovered.

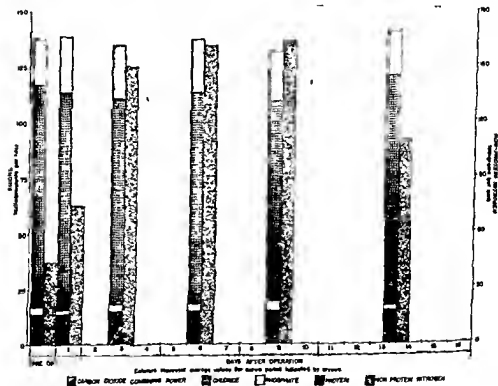


Fig. 1.—Plasma anions and nonprotein nitrogen average values for all cases in azotemia group.

In presenting the large number of blood chemistry and urine determinations carried out in these patients an attempt has been made to group them in such a way that the averages represent as far as possible the typical physiologic and biochemical alterations which take place during the acute period up to the time of death, or in those who lived through the recovery phase as long as we could follow them. Variations from this typical picture in individual cases will also be mentioned where these seem important. For complete records the reader is referred to the clinical case histories.

TABLE VII AVERAGE PLASMA NONPROTEIN NITROGEN AND PLASMA OF SERUM PROTEINS AND ELECTROLYTES IN PATIENTS WITH HIGH AZOTEMIA *

	PREOPERATIVE	POSTOPERATIVE DAYS				
		1	2 TO 4	5 TO 7	8 TO 10	11 TO 16
Plasma NPN (milligrams per cent)	47.1 ± 4.5 (21 cases)	72.8 ± 4.2 (31 cases)	141.1 ± 9 (54 cases)	182.2 ± 17.2 (49 cases)	175.5 ± 29.8 (13 cases)	127.6 ± 23.4 (10 cases)
Plasma carbon dioxide combining power (milliequivalents per liter)	21.8 ± 1.3 (21 cases)	24.9 ± 1.3 (20 cases)	25.6 ± 0.9 (47 cases)	23.6 ± 1.5 (24 cases)	21.4 ± 2.1 (11 cases)	19.5 ± 1.5 (8 cases)
Plasma chloride (milliequivalents per liter)	99.8 ± 0.8 (21 cases)	91.8 ± 0.9 (11 cases)	93.7 ± 1.0 (34 cases)	93.1 ± 1.0 (44 cases)	91.8 ± 0.7 (10 cases)	103.0 ± 5.3 (10 cases)
Plasma phosphate (milliequivalents per liter)	7.0 ± 0.7 (18 cases)	2.6 ± 0.2 (26 cases)	7.0 (43 cases)	3.7 ± 0.3 (26 cases)	4.7 ± 0.5 (9 cases)	7.0 (10 cases)
Plasma protein (milliequivalents per liter)	14.9 ± 0.1 (21 cases)	15.1 ± 0.1 (12 cases)	15.6 ± 0.1 (51 cases)	15.5 ± 0.2 (31 cases)	15.8 ± 0.3 (13 cases)	15.8 ± 0.3 (10 cases)
Serum sodium (milliequivalents per liter)	146.3 ± 3.7 (5 cases)	147.5 ± 3.7 (6 cases)	141.3 ± 2.5 (21 cases)	137.8 ± 5.1 (8 cases)	140.7 ± 4.4 (8 cases)	151.7 ± 5.7 (7 cases)
Plasma magnesium (milliequivalents per liter)	2.0 ± 0.1 (13 cases)	1.4 ± 0.1 (5 cases)	2.4 ± 0.3 (13 cases)	2.4 ± 0.6 (3 cases)	.3 (3 cases)	2.2 ± 0.3 (5 cases)

*The averages were obtained from determinations done on 73 patients with an NPN level of 65 mg per cent or over at some time during their course. Where more than one determination was done on a given patient during a postoperative group of days only one (the most abnormal value) was included in the averages. Standard errors of the mean are shown. NPN represents nonprotein nitrogen.

Vitrogenous Waste Products and Phosphorus

Nonprotein Nitrogen—Fig 1 is constructed from Table VII which represents average values in 'high azotemia' cases. Although the variation is rather wide in some groups, an adequate number of cases probably is included.

TABLE VIII AVERAGE PLASMA NITROGENOUS WASTE PRODUCTS AND PHOSPHORUS IN PATIENTS DYING IN UREMIA (MILLIGRAMS PER CENT)

DAYS AFTER WOUNDING	NONPROTEIN NITROGEN	CREATININE	URIC ACID	PHOSPHORUS
1	61 ± 10.3 (9 cases)	3.0 ± 0.24 (9 cases)	4.1 (1 cases)	4.2 ± 0.47 (8 cases)
2	118 ± 11.5 (13 cases)	4.4 ± 0.24 (13 cases)	7.3 ± 1.1 (5 cases)	4.1 ± 0.28 (12 cases)
3	132 ± 6.2 (16 cases)	6.3 ± 0.26 (16 cases)	12.8 ± 2.4 (8 cases)	5.8 ± 0.42 (14 cases)
4	178 ± 5.1 (11 cases)	8.1 ± 0.47 (16 cases)	12.9 (3 cases)	5.9 ± 0.36 (14 cases)
5	245 ± 18.9 (11 cases)	8.9 ± 0.53 (13 cases)	15.0 (1 cases)	7.1 ± 0.96 (12 cases)
6	251 ± 13.0 (8 cases)	9.5 ± 0.70 (9 cases)	13.4 (7 cases)	6.9 ± 0.22 (8 cases)
7	234 ± 26.1 (4 cases)	7.8 ± 1.87 (4 cases)	—	6.6 (7 cases)
8	253 (2 cases)	11.7 (2 cases)	—	7.1 (2 cases)
9	278 ± 16.0 (3 cases)	11.4 ± 0.44 (3 cases)	—	6.8 (3 cases)
10	314 (1 cases)	11.4 (1 cases)	—	7.7 (7 cases)
11	296 (2 cases)	10.3 (2 cases)	—	6.8 (2 cases)

to give a fairly representative picture during the periods shown. In general, nitrogen retention is already significant by the first postoperative day, increases rapidly during the first ten days, and then begins to decline.

As shown previously, most of the patients who die do so in the first ten days, therefore, the fall in the tenth to fifteenth days chiefly represents patients who recovered. In general, the nonprotein nitrogen level rose progressively to the day of death in those patients who died primarily of renal insufficiency (Table VIII, Fig 2). However, two patients (Cases 66 and 93)¹ who

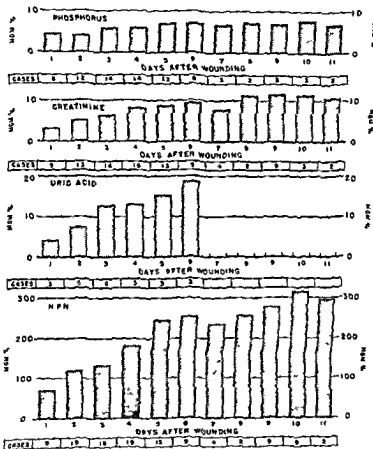


Fig 2—Average plasma nitrogenous waste products and phosphorus in patients dying in uremia (milligrams per cent)

lived longer than ten days after wounding fourteen and thirteen days, respectively) began to show some evidence of returning renal function. The significance of this fact in relation to therapy cannot be too strongly emphasized. It is important to avoid any measure which might precipitate death before this natural recovery can occur.

An attempt was made to determine whether the development of azotemia could be correlated with the degree of initial shock but this was not successful.

As mentioned previously, in the total number of patients who developed post traumatic azotemia oliguria or anuria, a large proportion had severe or moderate initial shock. A few patients developed renal insufficiency after slight shock or no shock (so far as we could determine) and the subsequent renal failure was as severe in these patients as in those with previous shock.

Similarly, there is no evidence that nonprotein nitrogen is initially higher in patients who subsequently die of uremia or develop oliguria or anuria, than in those who develop less severe renal failure.

Creatinine—Roughly the level of creatinine rose in the plasma as the total nonprotein nitrogen did (Fig 2 Tables VII and VIII)

Urea—Plasma urea nitrogen level was determined simultaneously with total nonprotein nitrogen in 15 cases (Table IX). Like creatinine it rose approximately as the total nonprotein nitrogen rose. The relationships of these three substances when nonprotein nitrogen is elevated are shown in the table. The averages were obtained by using thirty eight determinations from a larger series on 15 patients but including only those in which nonprotein nitrogen was over 100 mg per cent. If more than one determination was included from the same patient the individual samples were drawn at least twenty-four hours apart.

TABLE IX

	PLASMA AVERAGES (MG PER (CNT)			RATIOS (AVERAGES)	
	NONPROTEIN NITROGEN	UREA NITROGEN	CREATININE	UREA N P N	CREATININE N P N
Elevated*	193 ± 12	137 ± 9	7 ± 0.47	0.71 ± 0.01	0.033 ± 0.001
Normal	30	18	1.0	0.51	0.028

*Thirty eight determinations on fifteen patients

Although all waste products which make up the total nonprotein nitrogen rose in our patients these products did not accumulate in exactly the same proportions seen in the normal individual if these figures represent a fair sample.

Excretion of Urea and Creatinine—In 2 patients who died in the first five postoperative days twenty four hour urea nitrogen and creatinine excretion were measured. Table X shows the relations of the total amounts of these substances in the urine to plasma levels, urine specific gravity and urinary output.

The rising plasma level of nitrogenous waste products accompanied by urinary excretion in low amount of these same substances is distinctly shown. The falling output and low specific gravity of the urine are directly related to these changes.

Phosphorus—The well known retention of phosphorus in renal failure was present in our cases and in general paralleled the degree of nitrogen retention (Fig 2, Tables VII and VIII). In these patients with post traumatic azotemia, phosphorus retention is probably due primarily to impaired ability to excrete that substance. The hyperphosphatemia seen in patients in shock soon after wounding is due possibly to release of phosphates secondary to muscle damage.*

Relationship Between Calcium and Phosphorus—Twelve patients with azotemia had calcium and phosphorus determinations. The well known recip

TABLE V

	OUTPUT OF URINE (CC)	SERUM CREATININE OF URINE	Urea (PLASMA) (MG %)	UREA NITROGEN (URINE) (GM PER % URINE)	CREATININE (PLASMA) (MG %)	CREATININE (URINE) (GM PER % URINE)
<i>Case 108</i>						
<i>(Patient died in uremia)</i>						
Days of operation	100*	100*	7	0.1*	1.01	0.2*
First P.O. day	18	134	77	0.34	9	0
Second P.O. day	15	11*	11		5	0
Third P.O. day			10		6.15	
<i>Case 109</i>						
<i>(Uremia and convulsory case of leath)</i>						
Preoperative	60	1008	27		1.11	
First P.O. day	100	1017	41	"	1.61	1.0
Second P.O. day	1370	1019	46	9.4	1.64	1.0
Third P.O. day	1540	1015		1		1.35
Fourth P.O. day	800	1010	3	4.6	4.10	0.5
Fifth P.O. day			15*		9	

*Urine specimen represents nine hours only

†Specimens taken preoperatively on day of operation

TABLE VI

		PROS		DAYS POST OPERATION	OUTCOME
				4	Recovery of uremia
				14	
133	84	47	105	1	Recovery of uremia
	95	4	101	14	
60	99	50	55	8	Recovery of uremia
9	90	0	155	5	Death in uremia
	93	3	23	11*	
7	90	1	140	4	Recovery, never had of
					outlet
11	89	40	6		Recovered with normal renal failure
104	8	51	7	1	Death in uremia
5	84	109	54	81	Death in uremia
	77	1	101	5	
11	80	43	10		Death in uremia
8	8	49	18	4	Death in uremia
	7	6	91	5	Death in uremia
	4	5	166		Death in uremia
Averages for patients with Ca 9 or over (8 determinations)	7	54	15		
Averages for patients with Ca less than 9 (8 determinations)	81	7*	16		

*Days after crush injury

†Days after traumatic renal resection

total relationship between calcium and phosphorus is present in the majority of these cases (Table XI)

Uric acid—Uric acid like phosphorus and creatinine rose as the non protein nitrogen did in patients who developed azotemia; the same proportion of uric acid to total nonprotein nitrogen was roughly maintained while the retention of both was progressing with renal failure (Fig 2 Table VIII). The elevated uric acid seen soon after wounding and possible mechanisms for it have been discussed elsewhere.^{1, 2}

IONS —

Acid Base Balance

Plasma carbon dioxide combining power (and blood pH) The only group with a sufficient number of determinations for dependable averages was that of all the cases of high azotemia (Table VII). In these cases (Fig 3) initial low values were demonstrable followed by a rise toward normal on the first postoperative day. Throughout the next two weeks there was a gradual fall. Inspection of individual cases showed certain qualitative trends.¹ Patients with azotemia who had the most nitrogen retention, those who died in uremia and those with oliguria or anuria tended to have the lowest values. Conversely, the patients with the least nitrogen retention who lived and had normal output of urine tended to have normal values.

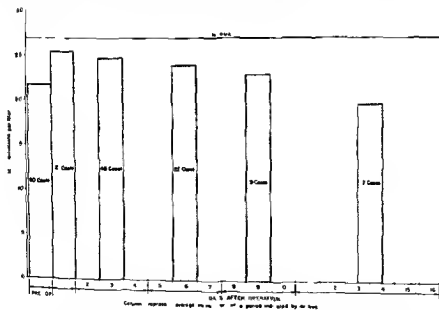


Fig 3—Plasma carbon dioxide combining power in azotemia

There is no correlation of combining power with degree of shock after the operative day. The acidosis seen in patients in shock on admission has been discussed.^{1, 2}

The evidence that a low carbon dioxide combining power is a result of diminished alkali reserve in these cases is only indirect. Blood pH's (venous)

TABLE XII

CASE NUMBER	PLASMA CARBON DIOXIDE COMBINING POWER (MEQ PER LITER)	BLOOD pH (VENOUS)
9.	16	7.21
60	23	7.29
112	20	7.04
133	21	7.32
20	20	7.37

were done in five cases that had low combining powers at the same time, and coincident renal failure (Table XII)

From this limited number of cases in which a pH was done and from the indirect evidence to be cited later it seems likely that at least in the majority of cases there was a metabolic acidosis present. If the low carbon dioxide were due to respiratory alkalosis one would expect to see clinical evidence of hyperventilation and an alkaline urine. None of our cases had either. Furthermore in such cases the blood pH although probably in the normal range would be in the upper limits of normal. Obviously we do not have enough pH determinations to draw any definite conclusions but the few we do have which are either within the lower limits of normal or below normal support the view that these patients in most cases were suffering from a metabolic acidosis. This was not of the hyperchloremic variety (See the section on chlorides and sodium)

Examination of Fig 4 and Tables VII and VIII gives at least a partial explanation for the acidosis. After the first postoperative day none of the patients were able to make a urine more acid than pH of 6.0 despite an increasingly severe acidosis. This is even more evident in the uremic death group in which the renal failure was most severe. Which portion of the base saving mechanism of the kidney is responsible for this can only be conjectured in most cases for it was possible to measure urine ammonia or titratable acidity in only a few instances. Likewise comparison of total anions with total cations gives little insight into the situation (see discussion of chloride and sodium)

TABLE XIII AVERAGE URINE pH IN THE HIGH AZOTEMIA GROUP

POSTOPERATIVE DAYS	POSTOPERATIVE DAYS			
	2 TO 4	5 TO 7	8 TO 10	11 TO 16
	5.0 ± 0.1 (-1 cases)	4.4 ± 0.1 (17 cases)	4.4 ± 0.1 (12 cases)	6.0 (2 cases)
	6.0 ± 0.1 (4 cases)	6.1 ± 0.1 (1 case)	6.0 ± 0.1 (11 cases)	6.3 ± 0.1 (10 cases)

Plasma chloride The plasma chloride level in the high azotemia group is shown in Table VII and Fig 5. In patients dying in uremia an extreme hyponatremia was reached by the tenth day if all cases are averaged and only one of these survived after the tenth day. This group (uremic death) is not, therefore represented in the column covering the eleventh to sixteenth days (Fig 5). Average values for patients who lived were only slightly low during the period of greatest nitrogen retention. Analysis of individual case

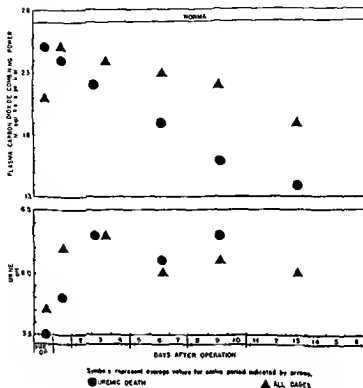


Fig 4—Plasma carbon dioxide combining power and pH of urine in azotemia

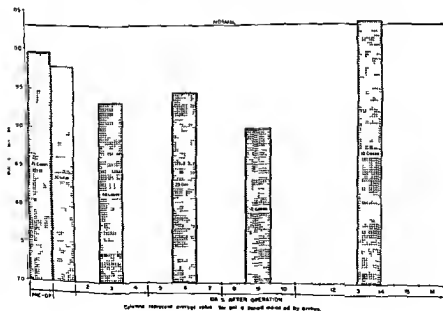


Fig 5—Average plasma chloride in azotemia

records showed that the patients with the lowest chlorides were chiefly those who died before the tenth day, and hence that the rise in the tenth to fifteenth days occurred largely in those patients who had had a recovery diuresis or minimal azotemia.¹

Relationship of low plasma chloride levels to intake of sodium chloride

Since, with the exception of a few cases with frank alkalosis, the hypochloremia in practically all instances was accompanied by a low carbon dioxide combining power, the mechanism of this hypochloremia was of considerable interest to us. Most of the patients with a low plasma chloride were extremely ill and took practically no food by mouth. Hence, their source of salt was almost entirely derived from that administered parenterally. Comparison of the amount of parenteral sodium chloride given to the patients who presumably had the most severe renal lesions in the group (those who died in uremia) with the corresponding plasma chloride level, shows interesting correlation (Table XIV). Of 32 patients who died in uremia 11 had normal chlorides up to the time of death. All of these 11 had received considerable parenteral sodium chloride in the previous three days. Twenty one patients had low chlorides under 107 meq per liter, and of these 21 10 had received no chlorides parenterally during the previous three days and 11 had received on an average much less salt than those with normal plasma levels. It should be emphasized that this analysis includes only patients who died in uremia and are therefore, those in whom the maximum degree of renal impairment could logically be expected.

TABLE XIV RELATIONSHIP OF PARENTERAL SODIUM CHLORIDE ADMINISTRATION TO PLASMA CHLORIDE

(a) In 32 patients who died in uremia and (b) in 19 patients who recovered (this group indicated by italics)

	TOTAL CASES	PLASMA CHLORIDE* (MEQ PER LITER)			PARENTERAL NaCl IN PREVIOUS 3 DAYS (GM PER DAY)			NO NaCl IN PREVIOUS 3 DAYS
		MAX	MIN	AVG	MAX	MIN	AVG	
Normal plasma chloride†	11	111	100	104	71.5	8.5	74.4	0
Number of cases	7	144	100	119	93.5	17.0	42.5	3
Low plasma chloride†	21	94	69	84.3	34.0	8.5	11.1	10
Number of cases	12	99	76	92.5	57.0	4.5	26.9	9
				21			11	
				12			3	

*Last determination only for Group (a) one to two days before death

† Normal 100 meq or over low under 100 meq

Patients who received no NaCl not included in average

In the patients with azotemia who survived the relationship of parenteral salt intake to low plasma chloride is not so clear cut (Table XIV). These patients as a whole were not so ill and probably their chloride intake by mouth was more nearly adequate therefore the parenteral salt received is not as accurate a measure of chloride intake as in patients who died in uremia. If one consults the individual records of patients who developed marked renal failure and yet survived (see also the section on Recovery Diuresis), it would

appear that hypochloremia is part of the chemical picture in most such cases (for example, Cases 60, 27, 125)¹ but that it is to a large degree associated with the sodium chloride intake. This relationship to intake is also brought out in conjunction with the discussion of sodium (see discussion to follow and Fig 6).

Several exceptions to these generalizations were evident in individual cases. With apparently adequate salt intake the chloride may be low, even in cases where there was no demonstrable loss of chloride through Wangensteen drainage or vomiting. In one case with azotemia and all the other clinical features common to the syndrome of severe renal failure the plasma chlorides were abnormally high (Case 133)¹ although here the salt intake had been excessive (Fig 7).

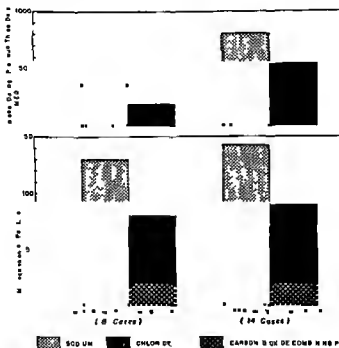


Fig 6—Relationship of serum sodium, plasma chloride and carbon dioxide combining power to parenteral intake of sodium and chloride in azotemia.

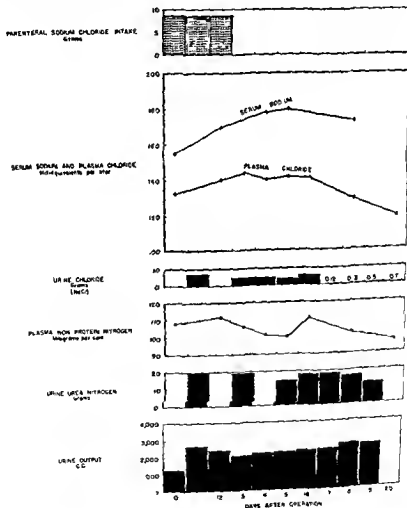
It is possible that the hypochloremia might be due in part to a simple dilution of the chloride ion for practically all of these patients had an increased plasma volume. (See discussion on Plasma Volume to follow). No such connection however is apparent in Table XV which shows plasma volume and plasma chloride determinations done simultaneously in 18 patients who died in uremia.

No correlation between degree of initial shock and plasma chloride level could be demonstrated.

Chloride excretion. Total urinary chloride excretion was measured in five patients with renal failure (Cases 104, 107, 108, 112, 133)¹. Three of these

also had severe alkalosis and are discussed in detail elsewhere.¹⁻⁴ These three all had extremely low chloride excretion. The remaining 2 both had recovery diuresis. Chloride excretion in one (Case 104) was essentially normal, but in this instance determinations were begun after he had actually recovered. The other (Case 133)¹ is discussed in detail in the section on recovery diuresis. In brief, he had hyperchloremia, but a high "threshold" for chloride excretion (Fig 7).

Chloride concentration of single specimens of urine was measured in 18 patients who died in uremia. In nine determinations on 8 patients with normal plasma chlorides (100 meq or over), the average urine chloride concentration was 124.4 ± 60.2 mg per cent. In 21 determinations on 10 patients with low



— Insufficiency and recovery diuresis
 elved 35 Gm. of sodium chloride
 & excretion of sodium chloride in

TABLE VI PLASMA CHLORIDE CONCENTRATIONS AND PLASMA VOLUMES IN EIGHTEEN PATIENTS WHO DIED IN UREMIA

CASE NUMBER	DAYS POSTOPERATIVE	PLASMA CHLORIDES (MG PER 100 ML)	PLASMA VOLUME (% INCREASE OR DECREASE)	BLOOD VOLUME (% INCREASE OR DECREASE)
9	6	72	43.9	21.0
69	8	76	27.5	15.8
86	6	76	61.4	23.5
55	7	80	95.1	37.7
47	3	82	33.6	8.8
93	6	82	22.2	6.1
118	5	87	16.1	6.1
80	4	84	10.7	-5.5
29	5	90	67.9	17.0
108	"	91	17.7	1.8
135	4	91	80.2	67.9
95	3	92	13.4	1.0
123	"	93	52.1	18.6
52	2	93	60.1	71.5
100	7	100	61.0	39.8
136	3	104	-19.7	-14.5
20	3	106	41.5	21.8
98	5	111	33.9	32.7

plasma levels the average was 326.0 ± 41.3 mg per cent, not a significant difference. It is difficult to say how important these single specimens are because of the well known fact that the chloride concentration of the urine varies widely throughout a twenty four hour period. The values in these groups of cases are undoubtedly lower than would be observed in normal individuals.

From the data presented it can be concluded that in renal failure of the type considered here the plasma chlorides tend in most cases to fall as renal insufficiency progresses. The degree of hypocholema depends to a large extent on salt intake. Measurements of urinary chloride indicate that the hypocholema is not due to excessive excretion of the chloride ion; indeed, the amount in the urine is below normal. No correlation between plasma level and increased plasma volume could be demonstrated, and therefore the low levels, as far as could be determined from our data were not due to simple dilution.

In addition to inadequate salt intake there must be other factors that contribute toward hypocholema such as a derangement of the chloride regulating mechanism which causes a shift of chloride ions from the intravascular bed to other extracellular or intracellular reservoirs. The fact that in these patients we demonstrated an abnormally large plasma volume would support such a hypothesis, although as stated previously no correlation of plasma chloride level with plasma volume *per se* could be demonstrated.

Plasma phosphate. The variations in phosphorus have been discussed under another heading in more detail (see the section on nitrogenous waste products). The phosphites are mentioned here again only to indicate their relation to total acid base balance. Reference to Fig. 1 and Table VII shows that when considered in terms of equivalence the plasma phosphates, even when elevated to twice normal or over make up a small proportion of the total anion column, they clearly account for only a portion of the carbon dioxide displaced in these cases.

also had severe alkalosis and are discussed in detail elsewhere.^{1, 6} These three all had extremely low chloride excretion. The remaining 2 both had recovery diuresis. Chloride excretion in one (Case 104) was essentially normal, but in this instance determinations were begun after he had actually recovered. The other (Case 133)¹ is discussed in detail in the section on recovery diuresis. In brief, he had hyperchloremia, but a high "threshold" for chloride excretion (Fig. 7).

Chloride concentration of single specimens of urine was measured in 15 patients who died in uremia. In nine determinations on 8 patients with normal plasma chlorides (100 meq or over), the average urine chloride concentration was 424.4 ± 60.2 mg per cent. In 21 determinations on 10 patients with low

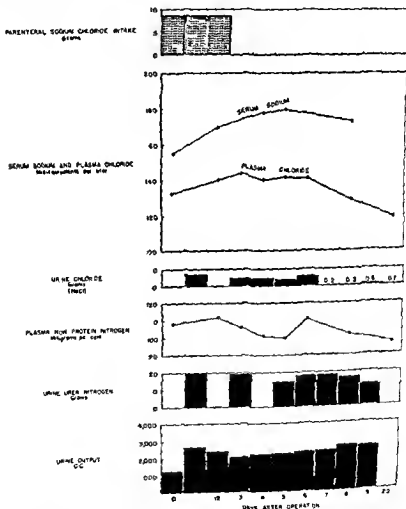


Fig. 7—Course of patient with post-traumatic renal insufficiency and recovery diuresis. During the six days previous to those depicted he had received 87 Gm of sodium chloride parenterally. Note hypernatremia, hyperchloremia, and low excretion of sodium chloride in spite of chloride and sodium retention in the blood (Case 133).

The cause of the acidosis in these cases was puzzling. If it were due to loss of total base one would expect a lower carbon dioxide combining power in the low sodium group. If due to substitution of chloride for carbon dioxide the plasma chlorides should be high. As mentioned previously phosphates are not sufficiently elevated to account for the change entirely in terms of base equivalence. Proteins remain constant and essentially normal. Sulfates and organic acids were not measured. These two components may account for some of the discrepancies evident in our data.

Magnesium. As with sodium there were too few determinations for statistical treatment. Fourteen determinations done between the second and tenth postoperative days in 13 cases (two determinations in the same patient on different days are included) averaged 23 ± 0.1 meq per liter. The nonprotein nitrogens done simultaneously averaged 164 ± 22 . If these few determinations were significant there was no evidence of abnormalities of magnesium metabolism in this type of renal insufficiency.

Potassium. Unfortunately only a few determinations were made. These are listed in the individual case records (Cases 78, 80, 107, 112, 133, 135, 138).¹ In five of these values were above normal (6.2 to 9.8 meq per liter).

Calcium. See the discussion on phosphorus under nonprotein nitrogen and phosphorus changes.

Plasma and Blood Volume

Plasma volume was determined in 23 patients at a time when they had posttraumatic renal insufficiency. The results were striking and of practical importance for they indicated that increase in plasma volume is a part of the abnormal physiologic picture.

Referring first to Tables XVII and XXII it is evident that in 19 fatal cases and in these fatal cases plus 4 with recovery diuresis the average plasma volume was increased significantly for the entire group $+41.6 \pm 6.6$ in fatal cases and $+43.3 \pm 5.7$ in all 23 cases. Average increases for those who received more than one liter of fluid intravenously daily (Group A) were much greater than for the 4 who received less than one liter daily (Group B, Table XXII). Analysis of Tables XXIII and XXIV from which the averages in Table XVII were computed shows that no patients in Group A and only one patient in Group B had normal or subnormal plasma volumes. In this one patient (Case

TABLE XVII. PLASMA VOLUME IN NINETEEN PATIENTS WITH FATAL ANURIA AND OLIGURIA. Figures Expressed as per cent of Calculated Normal Uncorrected Plasma Volume.

ALL CASES (19)		GROUP A (15 cases)		GROUP B (4 cases)	
INCREASE IN PLASMA VOLUME (AV)	DAYS AFTER OPERATION (AV)	INCREASE IN PLASMA VOLUME (AV)	DAYS AFTER OPERATION (AV)	INCREASE IN PLASMA VOLUME (AV)	DAYS AFTER OPERATION (AV)
41.6 ± 6.6	4.8 ± 0.4	41.1 ± 6.6	4.8 ± 0.5	1.5	4.8

Group A: Patients who received more than one liter of fluid (average) intravenous colloid and crystalloid per day.

Group B: Patients who received less than one liter of fluid (average) intravenous colloid and crystalloid per day.

Plasma Proteins Plasma proteins have been converted into milliequivalents in Fig 1 and Table VII. Inspection of these values shows a remarkable constancy with very small standard errors of the mean. Although the proteins represent a significant proportion of the total anions present, their importance in terms of change in acid base balance is negligible.

Cations —

Sodium The number of sodium analyses was small in comparison with those of anions. By grouping all determinations done in the patients with azotemia between the second and tenth postoperative days (or days after trauma), however, some interesting relationships emerged (Table XVI and Fig 6).

TABLE XVI. RELATIONSHIP OF SERUM SODIUM, PLASMA CHLORIDE, AND CARBON DIOXIDE COMBINING POWER TO PARENTERAL SODIUM AND CHLORIDE INTAKE IN AZOTEMIA

	AVERAGE LEVEL (MEQ PER LITER)			AVERAGE INTAKE DURING 3 DAYS PREVIOUS* (TOTAL MEQ)		
	SODIUM (SERUM)	CHLORIDE (PLASMA)	CARBON DIOXIDE (PLASMA)	EXTRA SODIUM	TOTAL SODIUM	CHLORIDE
Sodium under 140 (15 cases)	130.6 ± 1.2	90.4 ± 2.0	22.9 ± 1.8	157 ± 56	80.2 ± 6.0	183 ± 54
Sodium over 140 (14 cases)	146.5 ± 1.0	95.3 ± 2.7	23.0 ± 2.7	170 ± 43	66.0 ± 11.7	541 ± 9.0
All cases (29)	137.6 ± 1.4	92.7 ± 2.1	22.9 ± 1.3	163.5 ± 39	73.1 ± 7.5	339 ± 1

*Calculated from per cent of sodium or chloride present in sodium citrate, soda bicarbonate or sodium chloride.

The thirty-two determinations were done in 26 patients. In four instances two determinations in the same patient on different days are included and in one instance three determinations on different days. Twenty-four of the determinations were in patients dying in uremia; two were in cases where uremia was contributory to death and one was in a case where uremia was coincident with death. Five determinations were done in patients who survived 4 of whom had marked renal insufficiency. The table represents then a good sample of values for the electrolytes listed in post-traumatic renal insufficiency. Nine of the 14 with normal sodium died in uremia; 3 lived but had marked renal failure, and 1 had only slight renal failure. Sixteen of the 15 with low sodium died in uremia; 2 survived but had marked renal failure.

Several important facts seem evident from these data: (1) Serum sodium and plasma chloride concentrations are chiefly dependent on intake of these ions regardless of the severity of the renal insufficiency present. (2) The acidosis, as reflected by the low carbon dioxide combining power, is equally severe in either group, regardless of the sodium or chloride level. (3) The outcome was the same in both groups; there was no evidence that the diminished sodium and chloride concentrations in the plasma affected the course of the disease.

Table XX gives similar data on the 4 patients who had renal insufficiency and subsequent recovery diuresis. Fig 8 relates the plasma volume increase in 3 of them to nitrogen retention (Cases 60, 133, 138).¹ Plasma volume increased and then decreased as recovery diuresis proceeded and nitrogen waste products were excreted. The fourth (Case 150)¹ was seen for the first time after diuresis had begun although he still had marked renal failure. His plasma volume also was increased.

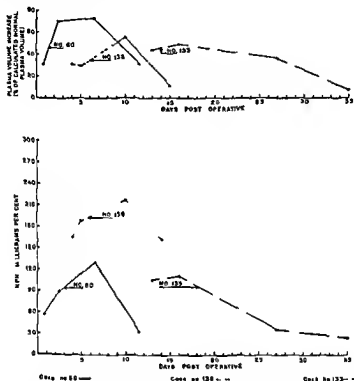


Fig 8—Plasma volume and plasma nonprotein nitrogen in recovery diuresis

Table XXI represents further analysis of all 23 cases. Twenty two had increased plasma volumes. Eighteen of these 22 received an average of more than one liter of crystalloid or colloid parenterally daily. In 10 of the 22, plasma volume was determined more than once and in 8 of these 10 plasma volume increased with increasing renal failure. In 3 cases with recovery diuresis included with these 8 plasma volume then shrank as renal function improved (Fig 8, Table XX). Of the 2 whose plasma volume did not increase as renal failure progressed one (Case 69 Table 18) was in Group A whose average fluid intake was high. His plasma volume was increased +23 per cent on both the second and ninth days after crushing injury. The other (Case 118, Table XIX) was in Group B those with restricted fluid intake. His plasma volume actually diminished although he subsequently died in uremia.

136) there is some reason to question whether deficient circulating blood volume was adequately replaced, and hence whether he ever really recovered from shock during the four days he survived after wounding

TABLE XVIII PLASMA AND BLOOD VOLUMES IN FATAL POST TRAUMATIC RENAL INSUFFICIENCY
Group A, Patients Who Received One Later or More of Intravenous Fluids
(Crystalloid or Colloid) Daily

CASE NUMBER	DAYS	PLASMA VOLUME (%)	PLASMA PROTEINS (gm %) (m %)	HEMATOCRIT (%)	BLOOD VOLUME (%)	BLOOD (UNITS)	PLASMA (UNITS)
105	1	67	51	28		11	3
	3	177	56	40	38	12	3
52	2		57	36		8	4
	3	601	62	38	235	8	4
55	6		64	27		6	6
	7	931	63	25	777	7	6
135	2	17*	65	20	229	6	0
	4	802	73	42	619	6	0
95	1		65	48		10	1
	3	134	66	40	-10	10	5
80	2		65	38		8	3
	4	107	71	38	-55	8	3
60	1*		68	70		10	5
	2*	235	63	52	186	15	12
	5*		54	47		13	12
	9*	235	51	42	158	15	12
47	1	87	53	33		45	2
	"	236	48	35	88	43	19
98	5	331	66	47	327	8	5
9	5		73	26		22	5.3
	6	409	68	37	21	22	5.3
86	2	265	60	33	61	8	2
	4		62	39		10	12
	6	614	61	32	235	10	12
106	7	610	73	29	208	2	0
114	0	752	58	30	319	6	1
26	3	415	69	38	218	45	6
123	3	523	58	42	186	7	11
	6		58	29		7.5	1.3

*Days after release from crush

†Since wounding

TABLE XIX PLASMA AND BLOOD VOLUMES IN FATAL POST TRAUMATIC RENAL INSUFFICIENCY

Group B, Patients Who Received Less Than One Later of Intravenous Fluids (crystalloid or colloid) Daily

CASE NUMBER	DAYS	PLASMA VOLUME (%)	PLASMA PROTEINS (gm %) (m %)	HEMATOCRIT (%)	BLOOD VOLUME (%)	BLOOD (UNITS)	PLASMA (UNITS)
93	1*	-314	73	60	-57	0	25
	3*		62	44		0	12
	8*	222	62	39	61	0	2
136	3	-193	80	50	-115	9	4
118	2	344	67	41	207	9	2
	5	16*	66	42	61	9	2
23	5	679	71	21	130	5	3

*Days after release from crush

†Since wounding

the absence of a dilution phenomenon is not evident from our data. One can only postulate that in such cases plasma protein was being mobilized from protein sources elsewhere in the body. The hematocrit in the 8 patients in whom plasma volume increased (as shown by serial determinations) rose in 1 (who received blood between measurements), was unchanged in 3 (2 of whom received blood between measurements) and fell in 4 (one of whom received blood between measurements). Although the total blood volumes were also increased, the increments clearly were a reflection of the increase in the plasma volume, and because of the low hematocrits in most cases were not as strikingly increased as the plasma volume.

These data indicate, then, that in this type of renal failure total circulating plasma volume is uniformly increased. This must be due largely to the inability of the kidneys to excrete adequate water. However, because the plasma protein concentration did not usually diminish as plasma volume increased, it is evident that the sole explanation is not simply that hydropnea exists. Unexplained extrarenal factors interfering with maintenance of a normal extracellular fluid volume seem also to be present. The practical importance of these observations is self-evident. Administration of excessive quantities of fluids to these patients who already have increased extracellular fluid volume can probably do nothing toward stimulating the kidneys to excrete; it can cause fatal pulmonary edema.

Changes in the Urine

Specific Gravity—One of the most striking and constant alterations in this syndrome is seen here. Within one or two days postoperatively the patients who developed renal failure almost without exception lost the power to make a concentrated urine regardless of the amount they were excreting (Fig. 9, Table XVIII). The averages listed in the table and those used in the figure were calculated from the specific gravities observed in routine specimens, usually the first morning specimens. They do not then represent true concentration tests, but there are several factors which indicate that the values observed in most cases are those of practically maximum concentrating ability. (1) Concentration tests were done later on patients who recovered when it was deemed safe to do so. In these, even after the retained nitrogenous products had been cleared and urinary output had returned to normal, specific gravity remained fixed and low for considerable periods of time. (2) Many of the specimens were taken when the urinary output was very low and hence when the kidneys

TABLE XVIII URINE SPECIFIC GRAVITY IN THE HIGH AZOTEMIA GROUP

Bed in uremia	PREOPERATIVE	POSTOPERATIVE				
		1	2 to 4	5 to 7	8 to 10	11 to 16
	1.033 (2 cases)	1.021 ± 0.002 (9 cases)	1.014 ± 0.001 (26 cases)	1.011 ± 0.001 (11 cases)	1.013 (4 cases)	1.011 (2 cases)
All cases	1.026 ± 0.002 (11 cases)	1.020 ± 0.001 (21 cases)	1.015 ± 0.001 (46 cases)	1.011 ± 0.001 (28 cases)	1.014 ± 0.001 (13 cases)	1.011 ± 0.001 (12 cases)

RECOVERY DIURESIS

The reasons for choosing arbitrarily the figure of 65 mg per cent of plasma nonprotein nitrogen as an index of renal insufficiency in this series of cases have been discussed. Of the 73 patients included in our high azotemia group 23 survived (32 per cent). These 23 may be further subdivided according to the degree of renal impairment they exhibited. Twelve had apparently only minimal interference with renal function with a rapid return to normal after transient nitrogen retention. We were unable to follow one patient with a nonprotein nitrogen greater than 65 and so do not know what degree of renal insufficiency he ultimately developed. Ten had more severe and marked abnormalities and conformed with the syndrome we have designated as recovery diuresis. The characteristic features of this syndrome are the presence of (1) a nonprotein nitrogen level greater than 100 mg per cent (2) oliguria or anuria followed by a substantial diuresis resulting in clearing of nitrogenous waste products and return to normal of the electrolyte pattern (3) impaired ability to concentrate the urine and (4) hypertension (systolic blood pressure above 135 mm of mercury diastolic above 90). Each of the 10 patients included showed at least three of these characteristics and most of them showed all four. One patient (No. 44)¹ was observed during a period when we were unable adequately to examine his blood and urine clinically, i.e. clearly conformed with the characteristics of the syndrome.

This small group of cases is of great interest and practical importance. One would like to know whereas the majority died why this group recovered and whether in their course in treatment there are any clues which might lead to more effective treatment than has been found to date. A detailed description of one or two of them and the results of search in the group as a whole for facts pertinent to their clinical and physiologic pictures will be presented. Complete records are presented elsewhere (Cases 21, 30, 43, 44, 60, 104, 121, 131, 138, 150).¹

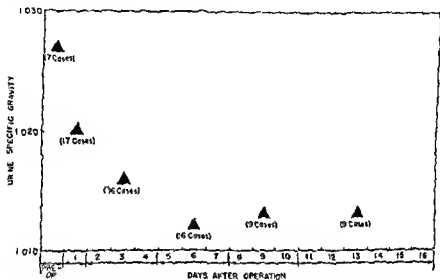
Clinical Features

The degree of initial shock was essentially the same as for the entire group that developed renal insufficiency. Three had severe shock, 5 moderate, 1 slight and 1 no shock. As in other cases it is quite possible that previous shock may have existed in all 10 but so far as we could determine 2 cases had to be classified as having slight shock and no shock respectively.

Five of these 10 patients had multiple major wounds. There were 6 peripheral wounds with fracture, 4 thoracic, 4 abdominal and 1 thoracoabdominal. There were no wounds of the liver or kidney. In one case there was contusion of the bladder.

The time of onset of oliguria in relation to wounding and operation and the duration of suppression of urinary output are of interest. Unfortun-

were theoretically concentrating urine to the maximum of their ability (3) In many of the patients, particularly those who died in uremia fluids were sharply restricted usually to about one liter a day—further reason for assuming that the average urine specimen would be concentrated if the kidneys were capable of making it so, although this last argument may be rendered untenable by the fact that plasma volume was probably increased in most such cases (4) Twenty four hour urine specimens were collected in 5 patients who developed renal failure In these the specific gravity of the total specimens showed the same trend, even though plasma nonprotein nitrogen was rising and, in 3 cases, total output of urine was diminishing



Symbols represent average values for entire period indicated by arrow.

Fig. 9—Urine specific gravity in patients with azotemia and oliguria or anuria

These data indicate that in this syndrome one of the earliest derangements of the kidney to appear and probably one of the last to disappear where recovery takes place is the ability to concentrate the urine

Hydrogen ion Concentration—The tendency of the acidity of the urine to decrease as metabolic acidosis and renal failure progress has been discussed (Table XIII, Fig. 4) From our meager data on measurement of titratable acidity and ammonia of the urine¹ it seems probable that the mechanism of this failure to make a very acid urine is due to a decrease in titratable acidity and thus is similar to that seen in most types of renal failure. Inability of the kidneys to make urine of maximum alkalinity if presented with a surplus of base, also seems to be a feature of the syndrome,² and again is similar to the situation occasionally seen in other types of kidney disease

significantly elevated with systolic levels ranging from 150 to 170 mm of mercury, and diastolic from 90 to 110. Likewise as diuresis progressed and non protein nitrogen fell, the blood pressures returned to normal. One patient was evacuated to the rear before hypertension had subsided and we were unable to obtain subsequent blood pressure determinations.

Two patients (Cases 44 and 150)¹ had generalized convulsions on the eighth or ninth postoperative days. In one, the convulsions furnished the first clue to the attending medical officers that renal failure was present. In one of

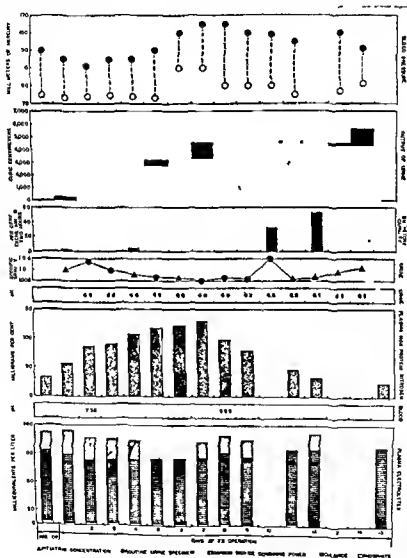
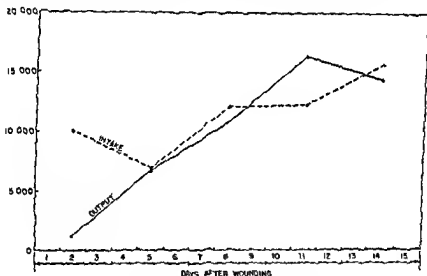


Fig. 12.—Course of patient with post traumatic renal insufficiency and subsequent recovery (Case 80).

nately the day to day records were not as accurate as one would like. Many of these patients were seen in field hospitals during periods of great military activity when the press of work made it extremely difficult to make such observations. We had no record of urinary output before the first postoperative day in any of these cases. Eight of the ten patients were known to have had at least one day of oliguria or anuria between the first and fifth postoperative days. Records of urinary output were not kept for 2 patients at the time they probably had oliguria but questioning of ward personnel and the patients suggested very strongly that they too were oliguric during this period. The duration of oliguria ranged from one to four days then followed a period of gradually increasing output of urine reaching in some cases 5 to 6 L. daily. The nonprotein nitrogen did not as a rule begin to decrease until several days after beginning of diuresis.



Points represent totals for first day periods.

Fig. 10—Intake and output of patient with post-traumatic renal insufficiency during course of recovery diuresis (Case 60).

Because of the increase in plasma volume during the azotemic period one would expect that total output would exceed intake during the diuresis period. This was clearly so in one case (Case 60)¹ discussed later (see Fig. 10) and in one other (Case 130)¹. In the remaining 8 cases it was impossible to demonstrate this fact from the available figures for the records kept gave only an approximate estimate of total water balance and did not account for water lost by perspiration, respiration or with stools. Since plasma volume returned to normal and the edema subsided as diuresis progressed it is logical to assume that total output does exceed intake until equilibrium is again established.

All patients had hypertension by our definition. In general the blood pressure was highest at the time of most severe nitrogen retention and was

significantly elevated with systolic levels ranging from 150 to 170 mm of mercury, and diastolic from 90 to 110. Likewise as diuresis progressed and non protein nitrogen fell, the blood pressures returned to normal. One patient was evacuated to the rear before hypertension had subsided and we were unable to obtain subsequent blood pressure determinations.

Two patients (Cases 14 and 150)¹ had generalized convulsions on the eighth or ninth postoperative days. In one the convulsions furnished the first clue to the attending medical officers that renal failure was present. In one of

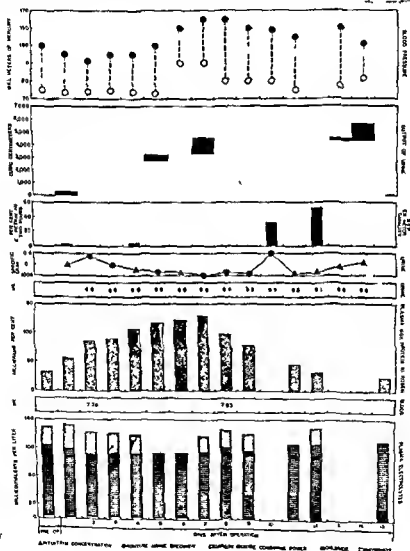


Fig. 11—Course of patient with post-traumatic renal insufficiency and subsequent recovery (Case 60).

the same two, there was a small retinal hemorrhage in the fundus of one eye. Eye grounds examined in 3 other cases were normal. In 4 cases there was clinical edema.

Blood Chemistry

The abnormal chemical pattern in this selected group of cases was essentially similar to that mentioned in the preceding section. Figs 10 and 11 (Case 60)¹ represent the course of one man and show the essential features seen in most cases. This patient who had had a period of severe initial shock was oliguric for one day. Renal function as measured by phenolsulfonphthalein excretion and the urine concentration test was extremely reduced by the first postoperative day and a gradual increase of urinary output followed. In spite of diuresis however, the nonprotein nitrogen continued to rise for the first seven days—apparently because with a fixed specific gravity of the urine the kidneys were unable to clear excess nitrogen until urine volume became great. Blood pressure rose and fell coincident with the degree of nitrogen retention. Electrolytes followed the pattern already described but returned to normal as renal function improved. Inability to make an acid urine in the presence of mild acidosis was evident. When this patient was evacuated on the fifteenth postoperative day renal function was still reduced despite normal chemical findings in the blood.*

The other 8 cases followed essentially the same pattern. The time of maximum nitrogen retention varied. 5 cases developed the highest nonprotein nitrogen between the third and ninth days after trauma and the remaining four between the tenth and thirteenth days. The period of time required for recovery hence varied from 6 to 25 days. As mentioned in the preceding section hypochloremia was not as marked a feature in these patients as in those who died in uremia. It was present to some degree in 5 patients (plasma chlorides under 100 meq per liter). One patient (Case 133) on the other hand following a very high intake of sodium chloride developed a marked hyperchloremia. The relation of plasma chloride serum sodium plasma carbon dioxide combining power fluid and sodium chloride intake urinary output and urinary excretion of chloride in this same patient are also shown in Fig 10. After an intake of 95 Gm of sodium chloride during the six days previous to those depicted sodium and chloride retention developed. Plasma carbon dioxide fell in this instance probably in part as a result of hyperchloremia. Chloride excretion was relatively low considering the high plasma level. As the plasma level fell chloride excretion decreased to negligible amounts during the last four days even though the amount of chloride in the plasma was still high. The hyperchloremia. There was a fall in sodium and chloride for both sodium and chloride in our hour urine specimens were uniformly dilute.

*Penal function studies done ten months later in the United States were normal.

Plasma Volume

Three of four patients with recovery diuresis whose plasma volumes were measured had significant plasma volume increase which was greatest at the time of maximum nitrogen retention and decreased as diuresis proceeded. They are discussed in a previous section on plasma volume and the courses of 3 are depicted in Fig 8. The fourth had normal blood volume when studied; this was after diuresis had started although he still had marked renal insufficiency.

Urine Specific Gravity

Five patients following administration of pituitrin were unable to concentrate urine above 1015 as long as they were followed (in one case up to forty nine days postoperatively). One patient with very transient nitrogen retention could concentrate to 1090 by the thirteenth day. Concentration tests were not done in the other four but several specimens in 3 cases were uniformly dilute. In one case (Case 30)¹ two routine specimens taken at the time of maximum nitrogen retention were 1019 and 1023.

Renal Clearances and Phenolsulfonphthalein Excretion

The results of tests for renal clearances and phenolsulfonphthalein excretion in patients with recovery diuresis are discussed in detail elsewhere.² Briefly in 3 patients in whom clearance measurements were made all functional components of the kidney were diminished when first observed but gradually returned toward normal over a period of several days or weeks. Similar evidence of functional impairment and subsequent improvement was seen in three patients in whom phenolsulfonphthalein excretory capacity tests were made.

TREATMENT OF POST TRAUMATIC RENAL INSUFFICIENCY

Introduction

It should be stated at once that treatment of this syndrome once it has developed proves disappointing. The cause of renal failure is discussed elsewhere. Evidence has been presented here that shock is one factor important in the etiology; once the patient becomes available for treatment it can usually be corrected fairly rapidly. Primary treatment should therefore be directed to the well known principle of prompt and adequate resuscitation of every man in shock.

Our experience and recommendations in the management of patients with post traumatic renal insufficiency, the therapeutic errors to be avoided and the questionable use of certain drugs and procedures to stimulate renal function will be presented.

Fluid Intake

Early in the Italian campaign fatal cases of post traumatic renal insufficiency began to appear. Therapy almost universally consisted of intravenous administration of large amounts of various crystalloids. Practically every known diuretic was employed in some cases. In addition attempts were often

made to render the urine alkaline by administering large quantities of available base by mouth or intravenously. In the absence of adequate urinary output the renal insufficiency soon became complicated by cardiac failure resulting from overload of the circulation. The majority of patients died rather promptly of pulmonary edema before they could die in uremia or (as might have been the case in a few) before they could regain adequate renal function.

Early in our study it was found that the majority of patients with post-traumatic renal insufficiency had increased plasma volume and that if more fluids were added especially those containing sodium water retention became even more severe. Thus the frequency of pulmonary edema and cardiac failure is not surprising.

The therapeutic implication of such physiologic abnormality is clear. Patients with this type of renal insufficiency already have too much extracellular fluid and too large a plasma volume. The abnormality must chiefly lie in the kidneys, which are not able to excrete this surplus water. Treatment should therefore include measures which might encourage the kidneys to excrete more urine but avoid any measures which would further increase plasma volume and secondarily cause cardiac embarrassment.

As described previously the critical period in most of these cases appeared to be the first ten days. Evidence has been presented that renal function did begin to improve spontaneously about the tenth day in some patients even though they subsequently died in uremia. The importance of avoiding an early fatal outcome as the result of too enthusiastic fluid administration cannot be overemphasized. Unfortunately most patients later died in uremia regardless of treatment. The judicious administration of fluids at least allowed them an opportunity to recover renal function spontaneously.

We felt that the total daily fluid intake of the average patient with oliguria or anuria should not exceed 500 to 1000 cc. Where extrarenal water losses are great however this allowance should be increased. If urinary output increases to more than one liter daily fluid intake should roughly parallel urinary output until retained nitrogen is cleared. Oral fluids where possible are preferable to parenteral fluids in order to avoid sudden augmentation of the hydremia. What parenteral fluids are used should be administered slowly. Careful observation for signs of pulmonary edema during infusion is clearly a necessity. Because of the water retaining property of the cation in sodium chloride we suggested that the bulk of administered parenteral fluid be 5 or 10 per cent glucose in distilled water. It now appears that by so doing salt deprivation occurred in some cases the outcome in those with hyponatremia however was not different from that in the group with normal chloride.

In patients where this regimen of fluid restriction was followed the incidence of pulmonary edema was in our considered judgment materially lessened in those who subsequently died primarily of renal failure. A few who recovered might have died of heart failure had they been given quantities of fluid comparable to earlier usage.

Procedures and Drugs Used to Stimulate Kidney Function

Our experience uncovered it may be reiterated no positive measures capable of surely re establishing kidney function—once renal insufficiency has developed. The aim should be to avoid measures that might be harmful before the kidneys begin spontaneously to clear retained waste products. Renal stimulating measures that have been tried will be described briefly here.

Hypertonic Solutions—The advisability of giving parenteral hypertonic solutions in this syndrome is highly debatable. They exert (at least in the presence of normal renal function) a diuretic effect by (1) increasing extracellular reservoirs and (2) limiting tubular reabsorption of water due to the osmotic effect of increased concentration of solute in the distal tubules. Increasing extracellular reservoirs is undesirable since circulating plasma volume already is abnormally increased. Limiting the tubular reabsorption may be beneficent if operative in the damaged kidney.

Hypertonic saline solution except in absolute amounts of salt necessary to maintain normal levels of sodium and chloride is contraindicated for excessive sodium would have a prolonged and undesirable effect on extracellular fluid volume. It was used (10 per cent solution of sodium chloride) in only one of our cases.

When parenteral fluids were given hypertonic glucose or 5 per cent glucose in normal saline solution was used in most of the cases we observed. The osmotic effect on extracellular fluid volume by solutions rendered hypertonic by sugar must be transient lasting only until the glucose is metabolized. This type of solution also serves a nutritive function in these patients who as a rule are eating poorly or not at all. The concentration of hypertonic glucose employed in our cases varied from 10 to 50 per cent the former being the most frequent.

There was little evidence however that the extensive use of these forms of hypertonic solutions had any effects upon urinary output. Since hypertonic solutions are ineffective in promoting urinary flow and may dangerously increase blood volume it would appear that the use of isotonic solutions is preferable. If hypertonic solutions are employed glucose is the choice. All hypertonic solutions are contraindicated in anuria.

Alcohol—Because of the known diuretic effect of alcohol and the suggestion that alcohol might increase renal blood flow a rather extensive trial of this agent was prompted. It was used in twenty patients who died primarily of renal insufficiency. The usual method of administration was to give it slowly intravenously in 5 per cent solution in total daily dosage of 50 to 100 cc of 95 per cent ethyl alcohol or if the patient could tolerate it to give 120 to 180 cc of whisky by mouth daily. Seven patients received approximately this dose for one day only, 9 for three to four days and 4 for five to eight days. In a few cases the use of alcohol was followed by an increase in urinary output. Inspection of charts on fluid intake and output however demonstrated that many patients even those clearly dying of renal failure produced varying and sometimes significant quantities of urine regardless of the type of therapy em-

ploved. One might be tempted to attribute increased urinary output in a few of these twenty patients to the alcohol they received. Similar increases were found in those who received no alcohol.¹

Two patients with recovery diuresis received alcohol in doses comparable to those mentioned previously, and 8 others with recovery diuresis received none.

The use of alcohol produced no symptoms other than occasional mild euphoria or drowsiness.

Mercurial Diuretics—Mercurpurin was given to 3 patients who subsequently died of renal failure. 2 received 2 cc and the third 1 cc. No diuretic effect was demonstrable.

Aminophylline—No demonstrable diuresis resulted from intravenous administration of 0.24 to 0.48 Gm of aminophylline to 4 patients who subsequently died of renal failure.

Inorganic Ions—The use of physiologic saline solution has been mentioned under fluid intake.

Sodium sulfate in isotonic solution (3.2 per cent) or hypertonic solution (4.2 per cent) was given to two patients in doses of 800 and 1000 cc respectively. No beneficial or harmful effects were noted. Both subsequently died in renal failure.

A combination of magnesium sulfate and potassium chloride was suggested as a means of reducing edema of renal tubular cells and hence perhaps promoting urinary flow. Magnesium sulfate was used in 4 cases. 3 to 8 Gm daily (as 10 per cent) solution intravenously and intramuscularly were given for periods of two to five days. Plasma magnesium levels were determined in 2 of these cases—8.5 mg per cent after 24 Gm of magnesium sulfate in four days in one case and 4.6 mg per cent after 8 Gm in two days in the other. This second patient received also 10 Gm of potassium chloride (0.5 per cent solution intravenously) at about the same time. No increase in urinary output was demonstrated in these 4 patients; all later died of typical renal failure.

Although no definite symptoms of toxicity were demonstrable in these patients the use of magnesium in such cases in the field may be dangerous. Administration of magnesium in the presence of renal failure results in rapid rise of plasma concentration of this ion. The danger of reaching toxic levels outweighs in our opinion any possible beneficial effect of magnesium.

We obtained no data on potassium levels reached in the one patient who received potassium chloride. This ion likewise exerts toxic effects *bona fide* and in our opinion it should not be used. The literature gives some evidence to support the contention that retained potassium may play a lethal role in uremia.⁶

Alkalies—The effect of alkalies in wounded patients is discussed in detail in another report.⁴ Alkalies usually in small doses were given to many of the patients with renal insufficiency. Eleven patients who later died in uremia were given between 10 and 20 Gm of soda bicarbonate daily for two days or more. Only in 2 of these was an alkaline urine observed. The dangers of adding sodium to the extracellular fluid have been discussed. Furthermore

the only reason for its administration is to produce an alkaline urine the therapeutic value of which is debatable. Despite the insolubility of certain pigment proteins in acid urine we observed no evidence that the use of alkalis has any place in the therapy of established post-traumatic renal insufficiency in fact their use may cause further harm.

Spinal Anesthesia—High spinal anesthesia was performed in two cases (Cases 47 and 135). In neither was a diuretic effect noted.

Kidney Decapsulation Sympathectomy—Kidney decapsulation and sympathectomy were performed in one case (Case 129) fifty-four hours after initial operation during which time he had put out 150 cc of urine. The right kidney was decapsulated and a perirterial sympathectomy performed. No effect was expected none was obtained. He died in uremia forty-eight hours later having excreted 180 cc of urine after this second operation.

Correction of Anemia

In cases where whole blood transfusions were indicated for the correction of severe anemia these were given. Relatively freshly stored blood was used to avoid possible pigment insult secondary to intravascular hemolysis of aged cells. No benefit or detriment to the already failing kidney was observed.

SUMMARY

The changes that begin to occur in the internal environment soon after trauma have been described in a preceding report.^{1,2} The consequences of these early changes upon the kidney have been reported herein. A man who has undergone severe trauma and the accompanying shock can be adequately resuscitated and successfully operated upon. The latent renal incompetency in this man whose kidneys were normal prior to wounding usually does not become manifest until two or three days after wounding. At this time there appear signs of failure on the part of the kidneys to withstand the initial insult the effects of which thus far his body has resisted with fair success.

The first clinical sign of impending renal failure in the majority of patients is suppression of urinary output. Of 73 patients with high azotemia (a plasma nonprotein nitrogen level of 6 mg per cent or higher at some time during their course) 27 had anuria (daily output of 100 cc or less) and 29 had oliguria (100 to 600 cc daily).

Mortality was high. Fifty patients (69 per cent) of 73 with high azotemia died. Twenty-one (47 per cent) of 45 with oliguria and 30 (91 per cent) of 33 patients with anuria had a fatal outcome.

Initial shock was observed in a large proportion of our cases (if one excludes special types of cases such as crush injuries reaction to incompatible blood transfusion and sulfathiazole crystalluria). Thus 86 per cent of the high azotemia group, 73 per cent of the oliguria group and 76 per cent of the anuria group had moderate or severe initial shock. These figures are undoubtedly too low for many men probably had shock before we saw them.

Death occurred within the first ten days after wounding in 48 of 51 patients (94 per cent) with fatal post traumatic renal insufficiency. If the wounded man can withstand this critical period apparent recovery of renal function begins, and he may survive. Evidence of this returning renal function appeared in a few of our patients toward the end of their course though they subsequently died in uremia. The importance of this fact should be emphasized, for therapeutic errors (such as overload of circulatory system by injudicious fluid administration) during this critical period may cause the fatal outcome before natural recovery can begin to take place.

Hypertension (systolic level of 135 mm Hg or over and diastolic level of 90 mm Hg or over) occurred in 62 per cent of the "high azotemia" group and in 79 per cent of the uremia fatalities within this group. Many of the patients who did not develop blood pressure elevation died within four days after wounding. Had they survived longer, probably they too would have developed hypertension.

The important biochemical and physiologic abnormalities in the blood resulting from post traumatic renal insufficiency are nitrogen and phosphorus retention, acidosis, hypochloremia and increase in plasma volume. These blood and plasma changes reflect rapidly diminishing renal function as indicated by inability to concentrate the urine by frequent failure to make a highly acid or alkaline urine in the presence of metabolic acidosis or alkalosis by diminished glomerular filtration and renal blood flow and by decreased phenolsulfon phthalein and maximum tubular excretory capacity of para amino hippuric acid.

The levels of plasma nonprotein nitrogen, urea, creatinine, uric acid and phosphorus rose as renal failure progressed during the first ten days after wounding. Most of the observations made after this period were in patients who recovered. These levels fell between the tenth and fifteenth days.

A progressive, fairly severe acidosis was characteristic manifested by falling plasma carbon dioxide combining power as renal failure progressed. A loss of ability to make a highly acid urine in most cases suggested that the acidosis could partially be explained by impairment of the mechanism which produces an acid urine. There was also good evidence that excretion of sodium in the form of sodium bicarbonate was poorly effected in those cases in which alkalosis resulted from excessive administration of base.

Hypochloremia was severe and progressive if all fatal cases are considered. Correlation of plasma chloride level and sodium chloride intake, however, demonstrated that the low chlorides were largely a result of inadequate salt intake. Serum sodium levels showed similar correlation. There was no difference in mortality between the hypochloremic and the normal chloride groups. One patient with renal failure had severe sodium and chloride retention following a high salt intake. Variations in plasma chloride levels were not entirely accounted for by intake. No correlation with degree of hydremia was apparent but it was suggested that in addition to the demonstrated relation to intake some interference with water and sodium chloride equilibrium was present.

Phosphates in terms of acid equivalence contributed toward but did not entirely account for the acidosis. Plasma proteins if converted to milliequivalents were normal and constant. Sulfates and organic acids were not measured but possibly could account for discrepancies in our anion determinations.

Cation determinations were few. It has already been stated that sodium levels were correlated with salt intake. Magnesium was not significantly elevated in most cases. Potassium was determined in too few cases for conclusions. Calcium in the few cases where determined showed a reciprocal relationship to rising phosphorus levels.

Total plasma volume was significantly elevated in 22 of 23 patients with post-traumatic insufficiency. Nineteen of these 23 died. Three patients with severe renal failure but with recovery diuresis had plasma volume increases which reached a maximum at the time of greatest nitrogen retention and decreased after diuresis. The degree of plasma volume increase was clearly related to fluid intake. The water retention appeared to be largely a result of administration of more fluid than the impaired kidneys could excrete. Comparison of plasma volume to total blood volume indicated that it was the plasma which was increased rather than all elements of the blood. The expected dilution of plasma proteins was not demonstrated in most cases. The practical importance of this physiologic abnormality has been mentioned.

Ability to concentrate the urine diminished rapidly as the syndrome progressed and specific gravity became fixed in all patients with any marked degree of renal failure. In patients who recovered it was the last function of the kidney that we measured which returned to normal. Since urine concentration probably takes place lower down the nephron than does excretion of mannitol, para-amino hippuric acid or phenolsulfonphthalein, the lag in recovery of water reabsorptive capacity may point to greater relative functional impairment of the lower nephron.

Ten of the 73 patients with high azotemia exhibited all the features of severe renal failure but they subsequently developed a diuresis and recovered. This fact re-emphasizes the importance of avoiding early fatal therapeutic errors, thereby affording the kidneys an opportunity for spontaneous recovery.

Therapy of post-traumatic renal insufficiency is chiefly one of prevention—early and adequate resuscitation of all patients suffering from shock. Once renal failure develops the avoidance of the therapeutic error of administering too much fluid and hence accentuating an already increased plasma volume becomes of prime importance. Types and amounts of fluids to be administered during the period when renal failure is most severe (usually the first ten days after trauma) have been recommended. No success has been met with in the use of drugs and procedures directed toward the promotion of urine flow or the improvement of kidney function. These unsuccessful measures included the use of hypertonic solutions, alcohol, mercurial and xanthine diuretics, solutions of various inorganic ions, spinal anesthesia and decapitula-

tion of a kidney. The essential feature in therapy appears to be that of tiring the kidneys and the organism over the critical period until natural recovery takes place. Procedures such as peritoneal lavage which attempt to remove waste products by routes other than the kidneys until these organs resume their function offer possibilities untried by us.

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IV EFFECTS AND USE OF ALKALIES IN TRAUMATIC SHOCK

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THE use of alkalies has been recommended by some as an adjunct to the treatment of shock for two reasons. First, it was proposed as a means of combating acidosis known to exist in shock; second it was suggested that production of alkaline urine might make more soluble abnormal blood or muscle pigments and sulfonamides as they were excreted in the urine. Evidence will be presented here that with judicious use of alkali it is possible to relieve metabolic acidosis, but that in the presence of shock and accompanying decrease in renal function it may be very difficult and even dangerous to attempt to produce an alkaline urine.

Any patient who receives blood or blood substitutes of necessity gets sodium citrate, which is employed as anticoagulant when the blood is collected from the donor. Although the amount varies slightly, we have assumed that each unit of blood or plasma contains 2.0 Gm. of U.S.P. sodium citrate. The amount of alkali given to a patient who receives several liters of blood or plasma is therefore considerable.

When additional alkali was given in the cases we observed, 2 per cent soda bicarbonate solution was the one usually employed. This was prepared by adding the soda bicarbonate to distilled water just as it was removed from the autoclave. Although some sodium carbonate undoubtedly resulted from this procedure, no untoward reactions were encountered in a large series of patients to whom this solution was given intravenously. Sodium citrate, 4 or 25 per cent, in sterile ampules was also employed in a few instances.

The sodium administered in excess of that given as sodium chloride was calculated from the amount present in sodium citrate or soda bicarbonate. This figure furnished a convenient index of total alkali received, since both citrate and bicarbonate were frequently administered.

In Table I the effect of increasing amounts of alkali in relation to the degree of initial shock is shown. Those patients who received between 1.0 and 5.0 Gm. of sodium (approximately 5 to 20 Gm. of sodium citrate or soda bicarbonate) still had an acid urine after twenty to thirty hours and showed no remarkable rise in plasma carbon dioxide combining power.

Those who received between 5.1 and 10.0 Gm. of sodium developed an alkaline urine only if they had slight or no initial shock. There was a signifi-

*This paper is published with minor changes from "The Physiological Effects of Wounds," a report of The Board for the Study of the Severely Wounded by the same authors (Government Printing Office, 1945).

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TABLE I. RELATIONSHIP BETWEEN INITIAL SHOCK TO PYRAMA CATION DIOL AND COMBINING POWER AND H₂O UPTAKE

[illegible]

The first part of the book is a history of the unit from its formation in 1942 to the present. It covers the unit's role in the Pacific Theater, its participation in the Battle of Iwo Jima, and its subsequent deployment to Japan. The second part of the book is a collection of letters and diary entries from the unit's members, providing a personal perspective on the war. The third part of the book is a collection of photographs and illustrations, including a map of the Pacific Theater and a photograph of the unit's headquarters in Iwo Jima. The book is a valuable resource for anyone interested in the history of the 28th Central Postal Directory.

Tables II, III, IV, and Figs 1, 2, and 3, which depict the sequence of events in three patients with moderate or severe shock who received large amounts of alkali

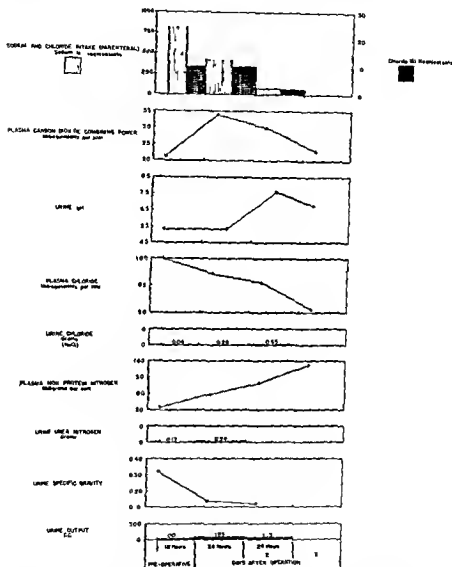


Fig 1—Effect of alkali in a patient who died of post-traumatic renal insufficiency (Case 108). The findings are discussed in the text. Note the lag in development of an alkaliotic urine in the presence of a relative alkalosis.

The first patient (Table II and Fig 1 (Case 108)), who had severe initial shock, received 34 Gm of sodium bicarbonate and 24 Gm of sodium citrate within the first twenty-four hours after entering the hospital. Plasma carbon dioxide responded to this excess alkali by rapidly rising to 34 meq per liter, but in

spite of this relative alkalosis the urine did not become alkaline until the second postoperative day. Plasma chloride fell in spite of practically no urinary chloride excretion. Coincident with these changes in acid base metabolism, urine output was very small, specific gravity of urine fell, plasma nonprotein nitrogen

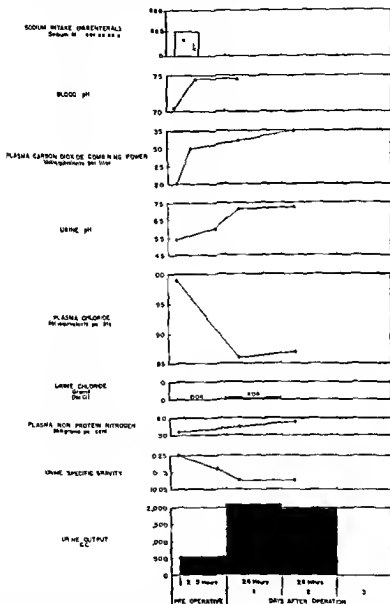
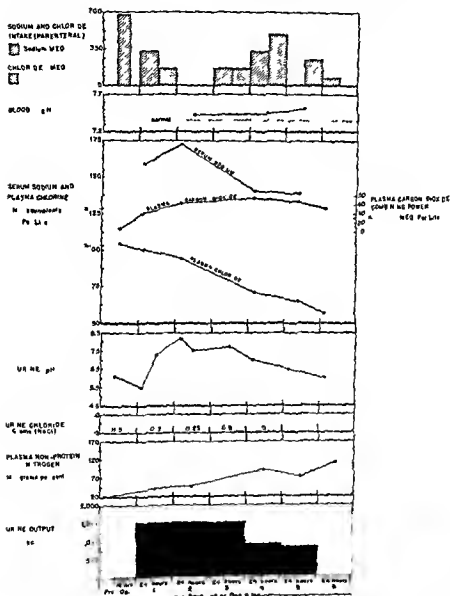


FIG. 2.—Effect of alkali in a patient with septic shock subsequent nitrogen retention and recovery (Case 1124). The findings are discussed in the text. Note (1) rapid metabolic response to alkali but delayed production of an alkaline urine; (2) continued alkalosis as long as followed; (3) low plasma chlorides and low urinary chloride excretion; (4) nitrogen retention; (5) a feebly alkaline urine output but low specific gravity and hence the rising plasma nonprotein nitrogen.

rose, urea nitrogen excretion was minimal, and the patient died in uremia on the third postoperative day.

The second patient (Table III and Fig 2 Case 112¹) received 20 Gm of soda bicarbonate and 16 Gm of sodium citrate within six hours after entering



112 p alkalosis
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the hospital in severe shock. Blood pH and plasma carbon dioxide combining power promptly rose to levels suggesting alkalosis, but the urine was not alkaline until nearly twenty four hours after the administration of alkali. Although urine output was normal after the first day, nonprotein nitrogen rose to 67 mg per cent by the second postoperative day when the patient had to be evacuated. Subsequent follow up revealed that nitrogen retention persisted for ten days, the status of the acid base metabolism could not be followed. Plasma chlorides likewise fell in this case and chloride excretion was very low.

TABLE IV. EFFECT OF ALKALI IN A PATIENT WITH MODERATE INITIAL SHOCK, POSTOPERATIVE ALKALOSIS, AZOTEMIA AND DEATH (CASE 107¹)

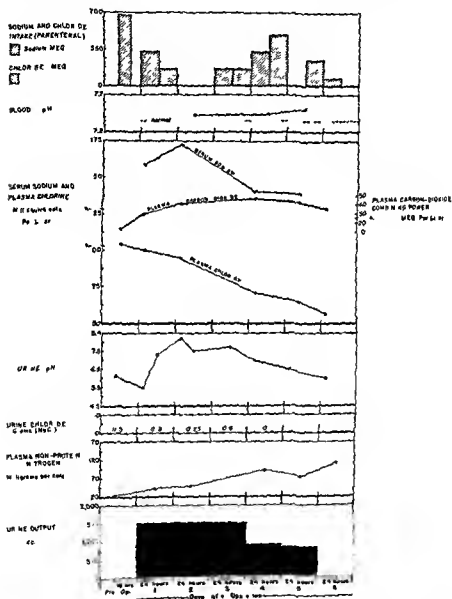
	PARENTERAL INTAKE		SODIUM (MEQ LITER)	CHLORIDE (MEQ LITER)	PLASMA CO ₂ (MEQ LITER)	BLOOD pH	URINARY NH ₄ (MEQ LITER)	PLASMA CHLORIDE (MEQ LITER)	URINARY CHLORIDE (MEQ LITER)
	Na (MEQ)	Cl (MEQ)							
Preoperative (18 hr)	681	0	15	103	61				60
First postoperative day	324	140	160	303	100	7.5		41	1,660
Second postoperative day	0	0	170	41	91	7.6	0.3	46	1570
Third postoperative day	146	140				7.7	0.23		1540
Fourth postoperative day	222	48	160	47	73	6.9	0.9	91	870
Fifth postoperative day	0	24	140	43	61	7.9	0.0	73	900
Sixth postoperative day	60	0		3	56	7.3		152	200(f)

The third patient (Table IV and Fig. 3 Case 107¹) admitted in moderate shock, received 35 Gm of soda bicarbonate and 28 Gm of sodium citrate on the day of operation, and 15 Gm more of soda bicarbonate early on the first postoperative day. The resulting severe and prolonged alkalosis was evident in the high plasma carbon dioxide and blood pH in spite of considerable ammonium chloride given on the fourth and fifth postoperative days. Here also there was a marked lag in the production of an alkaline urine after metabolic alkalosis appeared. By the fourth postoperative day although severe alkalosis persisted the patient was no longer able to excrete an alkaline urine. Plasma chlorides fell to phenomenally low levels in this case (56 meq per liter on the day before death) urinary chloride excretion was practically zero throughout the course. The nonprotein nitrogen rose and he died with renal failure as an important contributory factor, in our opinion on the sixth postoperative day.

The low plasma chlorides in all three of these cases are probably explained on the same basis as in other cases described elsewhere^{1, 2} and also by the fact that in the presence of high plasma carbon dioxide there has been a compensatory fall in plasma chloride. That this is not the entire explanation is evident in the fact that in two cases (Tables II and III Figs. 1 and 2) the plasma chloride continued to fall after plasma carbon dioxide had also begun to decrease.

rose urea nitrogen excretion was minimal and the patient died in uremia on the third postoperative day.

The second patient (Table III and Fig. 2 Case 112¹) received 20 Gm of soda bicarbonate and 16 Gm of sodium citrate within six hours after entering



112. 2nd postoperative alkalotic state (1) The lactate and lactic acidosis and postoperative (2) r. n. plasma in this case

the hospital in severe shock. Blood pH and plasma carbon dioxide combining power promptly rose to levels suggesting alkalosis but the urine was not alkaline until nearly twenty four hours after the administration of alkali. Although urine output was normal after the first day, nonprotein nitrogen rose to 67 mg per cent by the second postoperative day when the patient had to be evacuated. Subsequent follow up revealed that nitrogen retention persisted for ten days, the status of the acid base metabolism could not be followed. Plasma chlorides likewise fell in this case and chloride excretion was very low.

TABLE IV. EFFECT OF ALKALI IN A PATIENT WITH MODERATE INITIAL SHOCK POSTOPERATIVE ALKALOSIS, AZOTEMIA AND DEATH (CASE 107)

	PARENTAL INTAKE		SODIUM MEQ PER L	AMMONIUM MEQ PER L	PLASMA CL (MEQ PER L)	PNEPH	URINARY CHLORIDE (G)	PLASMA NPN (MG %)	URINE OUTPUT (CC)
	(G)	(L)							
Preoperative (16 hr)	—	—	—	—	103	61	—	—	60
First postoperative day	3.4	140	30	30	100	50 10 73 80	—	41	1560
Second postoperative day	0	—	10	11	91	—	0.3	46	150
Third postoperative day	140	14	—	—	—	—	0.3	—	1540
Fourth postoperative day	3.0	45	10	47	73	68	0.5	91	870
Fifth postoperative day	—	0.4	140	43	6	58	0.0	3	800
Sixth postoperative day	6	0	—	—	56	73	—	152	200(?)

The third patient (Table IV and Fig 3 Case 107¹) admitted in moderate shock received 35 Gm of soda bicarbonate and 28 Gm of sodium citrate on the day of operation and 15 Gm more of soda bicarbonate early on the first postoperative day. The resulting severe and prolonged alkalosis was evident in the high plasma carbon dioxide and blood pH in spite of considerable ammonium chloride given on the fourth and fifth postoperative days. Here also there was a marked lag in the production of an alkaline urine after metabolic alkalosis appeared. By the fourth postoperative day although severe alkalosis persisted the patient was no longer able to excrete an alkaline urine. Plasma chlorides fell to phenomenally low levels in this case (56 meq per liter on the day before death) urinary chloride excretion was practically zero throughout the course. The nonprotein nitrogen rose and he died with renal failure as an important contributory factor in our opinion on the sixth postoperative day.

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SUMMARY AND CONCLUSIONS

The arguments in favor of the use of alkalis in shock are (1) to relieve metabolic acidosis and (2) to produce an alkaline urine. In our experience large amounts of alkali are necessary to relieve acidosis where severe that is in patients with shock. If, in addition, enough extra base is given to produce an alkaline urine in these same patients the margin of safety between normal acid base equilibrium and an uncompensated alkalosis may be very small. In the event that alkalosis does result it may contribute materially toward renal failure. Three instances in which this situation may have occurred have been presented.

The mechanism of the low alkali tolerance in these patients is probably similar to that occasionally evident in other types of renal insufficiency: the impaired ability of the kidneys to excrete excessive amounts of sodium as sodium bicarbonate is associated with the over all decrease in renal function which probably exists in all patients suffering from shock and even for some time after shock is relieved.^{1,2}

Because evidence that an alkaline urine does prevent renal complications in the type of patient we have studied is so scanty and because of the previously mentioned dangers inherent in trying to produce an alkaline urine we do not recommend giving alkali for the purpose of raising pH of the urine as a therapeutic procedure. Smaller amounts of alkali sufficient to relieve metabolic acidosis if judiciously employed are probably advisable. The obligatory amount of alkali given with blood or blood substitutes will in most instances be adequate for this purpose.

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Book Reviews

Diseases of the Chest With Emphasis on X ray Treatment By Eli H. Reuben Philadelphia, 1947, W. B. Saunders Company

From the title of the book, one would imagine that most of the consideration would be of roentgenology. This is certainly not so, because, although the roentgenographic examination of chest lesions is emphasized, the consideration of the various disease entities in the chest is taken up from every standpoint which, of course, makes the book more valuable. The first two chapters are devoted to the anatomic consideration of the normal roentgenographic findings of the chest and the technique of x ray examination. The third chapter is an excellent one on respiration in health and disease. This is concerned largely with physiology of respiration and methods of examination, such as vital capacity, bronchopneumetry, and the importance of each of these. Another chapter is devoted to the symptoms and physical findings of chest diseases in general, with emphasis upon the necessity of obtaining a good history and getting a complete physical examination.

The various disease processes affecting the lung are then taken up in detail, giving the etiology, clinical findings, and roentgenographic findings as far as diagnosis is concerned and the treatment. An interesting part of the work are the colored illustrations by Netter. Although some are diagrammatic, they are excellent and demonstrate the points very well. Following each chapter is an excellent bibliography containing the subject material discussed within that chapter. Interspersed in the chapter are many roentgenograms showing the x ray changes found in the particular condition being discussed. These are reproduced very well.

Tuberculosis is particularly well handled. An entire chapter is devoted to the epidemiologic considerations of tuberculosis. The fact that practically one fourth of the whole book is devoted to tuberculosis shows the relative importance of this disease and the complete manner with which it is considered.

The final section of the book is devoted to principles of surgical treatment, in which the surgical therapy of the various conditions are considered somewhat in detail. The book is excellently done and because of its completeness should be a reference book in every library.

Grandes Problemas de Clinica Quirúrgica By Alfredo Velasco S. Iaper Pp 431, with 33 illustrations. Santiago, Chile, 1943 Central de Publicaciones

This South American textbook of surgery is a collection of lectures given to students by the author and collaborators. The work reflects the views and experience of the group at the Clinic of Professor Alvaro Covarrubias of Santiago, Chile.

Beginning with a lengthy discourse on infection in general, it covers a wide variety of surgical subjects under thirty one chapter headings such as acute appendicitis, goiter, fractures of the neck of the femur, Buerger's disease or thromboangitis obliterans, cancer of the thyroid etc. Over one quarter of the book is devoted to infection, with the result that many subjects of considerable surgical significance are not even mentioned. Among the conditions omitted are breast disease, cancer of the lung and other surgical diseases of the lung with the exception of hydatid cyst of the lung, surgical affections of the mediastinum, heart, and pericardium, herniation, and preoperative and postoperative care. The various chapters are not in order so that certain subjects, such as orthopedics, are dispersed throughout the book. The book has an excellent table of contents but lacks a subject index. Every subject discussed is followed by a pertinent summary but no references are given.

The authors have used a novel approach in that most chapters begin with an illustrative case of the condition about to be discussed, this device enables the student to grasp quickly the problems that arise in the management of such a case and heightens the interest in the subsequent discussion. The work is written in a delightful conversational style and it aims to teach the student to observe, think, and reason things out for himself.

The best chapters in the book are those dealing with the thyroid gland and its diseases. The material is quite up to date and offers a concise review of the latest advances in this field. About the only inaccurate statement found in this section is that aberrant thyroid tissue is of no importance. Most surgeons now feel that aberrant thyroid tissues especially lateral aberrants, are likely foci of malignancy.

This book contains a great range of concentrated, worth while information and should receive wide use as a textbook in our neighboring Spanish speaking countries where there is a dearth of good medical textbooks in Spanish.

Announcement

Research on Orthopedic Appliances at Mellon Institute

Announcement has been made by Harold P. Weirlein, Director, Mellon Institute, Pittsburgh, Pa., of the establishment there of a comprehensive multiple research fellowship on orthopedic appliances by the Sarah Mellon Weir Foundation of Pittsburgh. The program will be planned and carried out for the benefit of mankind through the medical profession.

Under the guidance of orthopedists and with the cooperation of leading organizations in the field as well as of manufacturers of orthopedic appliances, the fellowship will conduct broad scientific investigation and development relating to such appliances. Particular attention will be accorded to problems of mechanical design, improvements in materials of construction and methods of fitting braces and similar orthopedic devices.

John L. Young, Ph.D., heads the program as Senior Fellow. A research specialist in metallurgy and mechanical engineering, he has been a tire on the investigatory staff of Mellon Institute since 1923. Eugene J. Murphy, M.E., Staff Engineer, Committee on Artificial Limbs, National Research Council, Washington, D.C., will serve as Advisory Fellow. Several research assistants will complete the initial personnel of the fellowship whose adviser on the executive staff of the Institute is the late H. Young, Assistant Director.

The medical advisory committee of the fellowship is under the chairmanship of Paul H. Steele, M.D., Professor and Head of the Department of Orthopedic Surgery, School of Medicine, University of Pittsburgh. The other members of this committee at the inception of the work are John A. Heberling, M.D., Associate Professor of Orthopedic Surgery, and Carl C. Young, M.D., Assistant Professor of Orthopedic Surgery in the same institution.

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